A Dissertation on

A STUDY OF CLINICAL PROFILE OF ATRIAL FIBRILLATION AND ITS TRANSTHORACIC ECHOCARDIOGRAPHY PRESENTATION A CROSS SECTIONAL STUDY AT A TERTIARY CARE HOSPITAL IN CHENNAI

Submitted to

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY
CHENNAI – 600032.

In partial fulfilment of the Regulations
for the Award of the Degree of

M.D. BRANCH - I

GENERAL MEDICINE

DEPARTMENT OF GENERAL MEDICINE
GOVERNMENT KILPAUK MEDICAL COLLEGE AND HOSPITAL
CHENNAI – 600 010
APRIL 2017

CERTIFICATE

This is to certify that Dr.**G.AMBEDKAR**, Post Graduate Student (2014-2017) in the Department of General Medicine, **GOVERNMENT KILPAUK MEDICAL COLLEGE AND HOSPITAL**, Chennai-600010,has done this dissertation on **"A STUDY OF CLINICAL PROFILE OF ATRIAL FIBRILLATION AND ITS TRANSTHORACIC ECHOCARDIOGRAPHY PRESENTATION A CROSS SECTIONAL STUDY AT A TERTIARY CARE HOSPITAL IN CHENNAI"** under our guidance and supervision in partial fulfilment of the regulations laid down by the Tamilnadu Dr.M.G.R. Medical University, Chennai, for M.D. (General Medicine), Degree Examination to be held in April 2017.

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DECLARATION

I, **Dr.G.AMBEDKAR** declare that I carried out this work on **"A STUDY OF CLINICAL PROFILE OF ATRIAL FIBRILLATION AND ITS TRANSTHORACIC ECHOCARDIOGRAPHY PRESENTATION A CROSS SECTIONAL STUDY AT A TERTIARY CARE HOSPITAL IN CHENNAI"** at Department of General Medicine, Government Kilpauk Medical College and Hospital during the period of April 2016 to September 2016. I also declare that this bonafide work or a part of this work was not submitted by me or any other for any award, degree, and diploma to any other university, board either in India or abroad.

This is submitted to The Tamilnadu Dr.M.G.R. Medical University, Chennai in partial fulfilment of the rules and regulation for the M. D. Degree examination in General Medicine.

Dr.G.AMBEDKAR

ACKNOWLEDGEMENTS

I am very much thankful to Prof.**Dr.R.NARAYANA BABU M.D,DCH**,THE DEAN,Govt.Kilpauk Medical College& Hospital, Chennai for granting me permission to utilize the facilities of the hospital for the study.

I express my profound thanks to my esteemed Prof. **Dr.S.USHALAKSHMI, MD**., Professor and HOD of General Medicine, Govt. Kilpauk Medical College& Hospital, for encouraging and extending her valuable opinion to perform and complete this dissertation.

I immensely thank my unit chief and guide Prof. **Dr.C.HARIHARAN M.D**., Professor Of General Medicine, Govt. Kilpauk Medical College &Hospital, for his constant guidance and encouragement throughout the study.

I am also immensely grateful to Prof. **Dr.C.MOORTHY, M.D., D.M**., Professor and HOD of Cardiology, Department of Cardiology, Govt Kilpauk Medical College& Hospital for his valuable guidance in conducting this study.

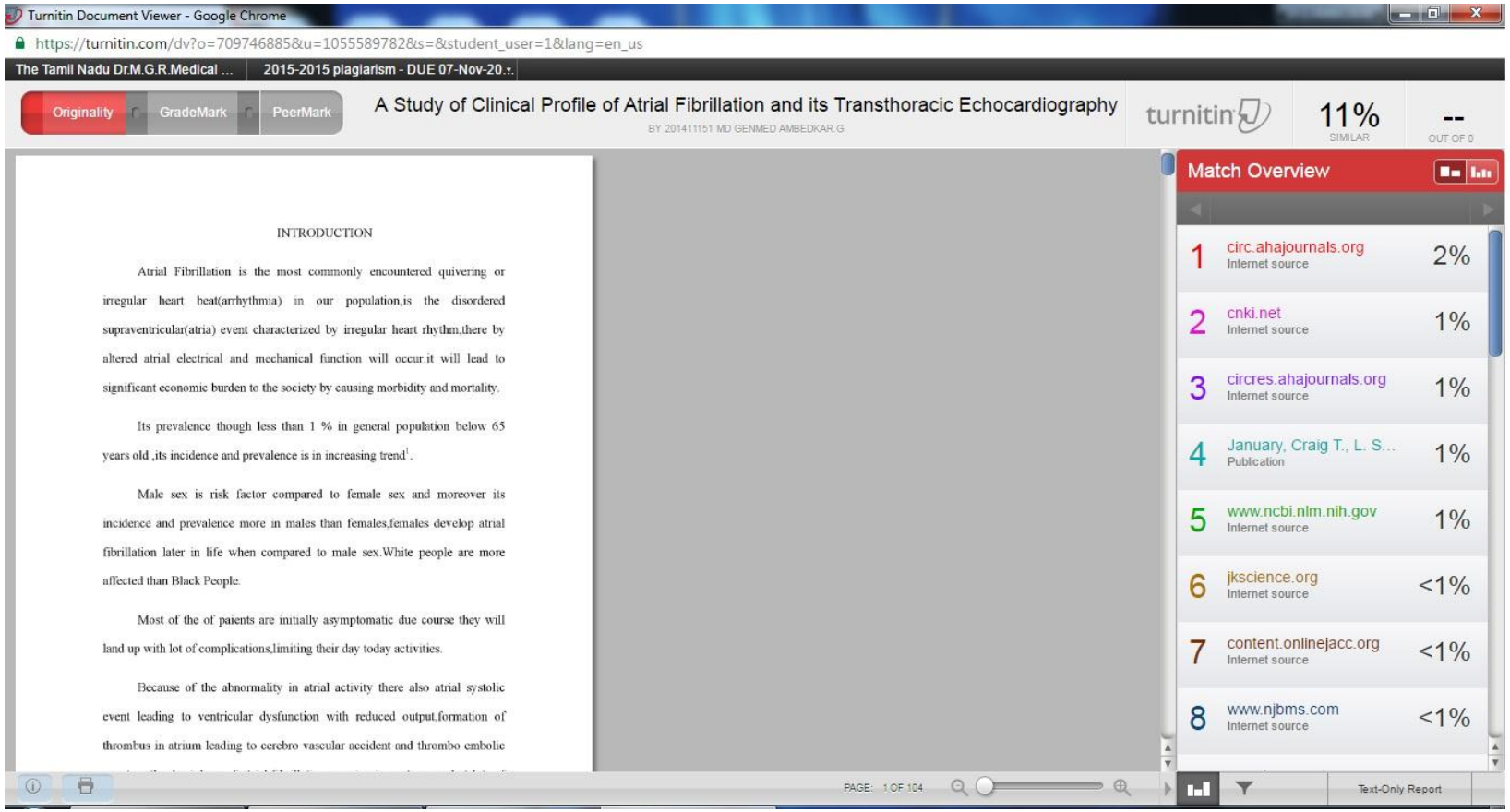
I wish to thank **Dr.G.GURUNAMASIVAYAM M.D (GM)., DPM, Dr. M. PRASANNAKUMAR M.D,** Assistant Professors of my unit, Department of General Medicine ,Govt Kilpauk Medical College& Hospital for thier valuable suggestions, constant support, encouragement and advice in doing this study.

I wish to thank**, Dr.P.SURESHKUMAR M.D., D.M,**, Assistant Professor ,Department of Cardiolgy,Govt Kilpauk Medical College& Hospital for his constant guidance and suggestions since the very beginning and till completion of my study.

I sincerely thank the members of Institutional Ethics Committee, Govt. Kilpauk Medical College &Hospital for approving my dissertation topic. I thank all our Post Graduates, House Surgeons, and Staffs of our Hospital for their contribution in this study. I thank **Mr. S. Venkatesan**, Statistician for his guidance in analysing this study. I express my gratitude to all the patients without whose cooperation this study would not have been successful.

Last but not least I thank my parents, my wife **Dr. G. Aruljothi M.B.B.S**., my child **A. Aparna** and my friend **Dr. A. Karthik M.D.,** for their constant support and encouragement.

Above all I wish to thank God, who has been my source of strength and to whom I owe everything.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INTRODUCTION
Atrial Fibrillation is the most commonly encountered quivering or irregular heart beat(arrhythmia) in our population,is the disordered supraventricular(atria) event characterized by irregular heart rhythm,there by altered atrial electrical and mechanical function will occur.it will lead to significant economic burden to the society by causing morbidity and mortality.
Its prevalence though less than 1 % in general population below 65 years old ,its incidence and prevalence is in increasing trend[1].
Male sex is risk factor compared to female sex and moreover its incidence and prevalence more in males than females,females develop atrial fibrillation later in life when compared to male sex.White people are more affected than Black People.
Most of the of paients are initially asymptomatic due course they will land up with lot of complications,limiting their day today activities.
Because of the abnormality in atrial activity there also atrial systolic event leading to ventricular dysfunction with reduced output,formation of thrombus in atrium leading to cerebro vascular accident and thrombo embolic
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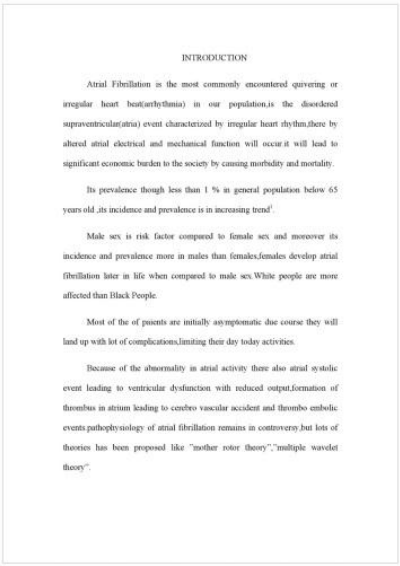

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CONTENTS

ABBREVIATIONS

AF	**:**Atrial fibrillation
CAD	:Coronary heart disease
HF	:Heart failure
IVSd	:Interventricular septal thickness in diastole
LVIDd	:Left ventricular internal diameter(cm) in diastole
LVIDs	: Left ventricular internal diameter(cm) in systole
LVPWDd	: Left ventricular posterior Wall diameter(cm) in diastole
OSA	:Obstructive sleep apnoea
PE	:Pericardial effusion
PHT	-Pulmonary hypertension
RHD	:Rheumatic heart disease
TRPG	:Tricuspid regurgitation peak gradient
TTE	:Transthoracic echocardiogram
TEE	:Transesophageal echocardiogram

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There are so many diseases are contributing to the development of atrial fibrillation among them Rheumatic valvular heart disease, Systemic hypertension, Ischemic heart disease are very important. Smoking and alcohol consumption are risk factors adding to the development of this dysrhythmias.

There are different types atrial fibrillation causes can be defined, but in undetermined or Lone AF no cause can be found.

Different diseases contributing to atrial fibrillation will appear at different ages, atrial fibrillation appearing because of valvular heart disease appears earlier than other diseases contributing to the development of atrial fibrillation.

ECG Shows irregular rhythm with normal or rapid rate, absent P waves, normal QRS Complex.

Main treatment modality is pharmacological, non pharmacological treatment options reserved for some patients. Newer drugs and Approaches under study.

Investigations are done to find out causes for atrial fibrillation and guide the clinicians for treatment strategies.

Echocardiography is useful to find out the causes for development of atrial fibrillation and various echocardigraphic parameters predicts risk for future development of atrial fibrillation and complications associated with atrial fibrillation.

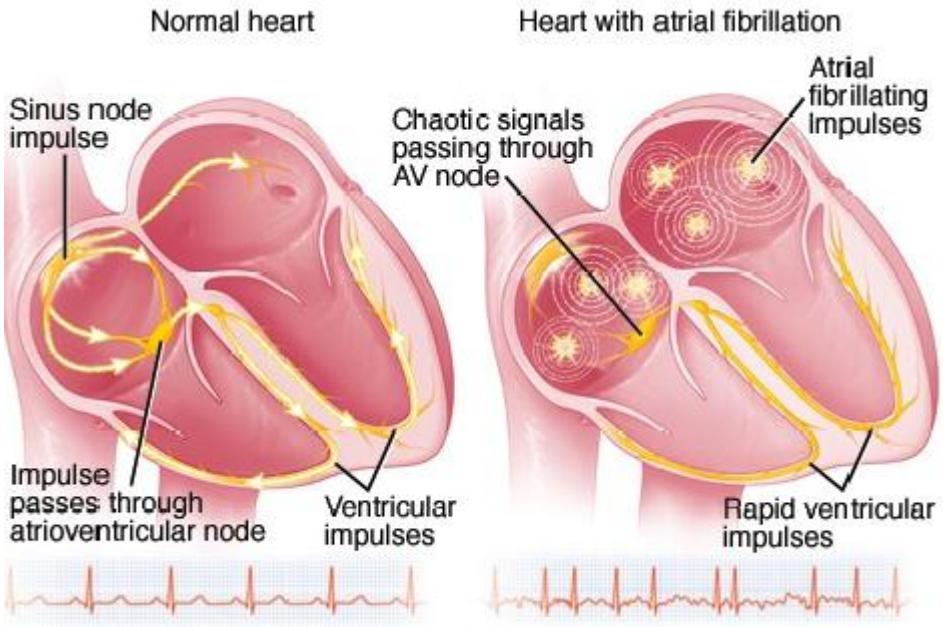
AIMS AND OBJECTIVES

1. To find out the varied presenting symptoms of Atrial fibrillation,
2. To find out possible underlying predisposing factors for Atrial fibrillation, both cardiac and non-cardiac in our population,
3. To perform Transthoracic Echocardiography and analysis of its parameters in Atrial fibrillation patients.

REVIEW OF LITERATURE

DEFINITION:

Atrial fibrillation is a Supraventricular tachyarrythmia with uncoordinated activity of atria characteristically resulting in disordered atrial mechanical and electrical function[1].Electrocardiographically characterized by low amplitude baseline oscillations called as Fibrillatory or 'F' waves and an irregularly irregular rhythm of ventricles with the rate of 300 to 600 beats per minute and they are variable in amplitude, shape, timing.



HISTORY:

Atrial fibrillation has the rich history that has touched the careers of many great clinicians and investigators of 20th century[2].

The first description of atrial fibrillation was mentioned in "Harmony and Health in the Huang Ti Nei Ching Su Wen"(The Yellow Emperor's Classic

of Internal Medicine).He is the physician emperor who ruled country china between 2697-2597 B.C[3].Even though it was described in ancient period, everybody came to know about a term "Fibrillation" after demonstration by William Harvey(1578-1657) in animals the fibrillation of auricles.Jean Baptist de Senac(1693-1770) described relationship between palpitation and stenosis of mitral valve.

In 1827 "Dublin Master of Clinical Expression" Robert Adams (1791-1799) mentioned about the association of irregular pulse and mitral stenosis. Digitalis leaf discovered in the year 1785 which gives relief to patients with congestive heart failure and atrial fibrillation, reported by William withering(1741-1799).

The first person who published human ECG depicting atrial fibrillation was William Einthoven(1860-1927) in the year 1906.Sir Thomas Lewis(1881-1945) "Father of modern ECG" who described about elctrophysiological characteristics of AF that its basic mechanism is circus movement of electrical impulse that is "Re-entry". In the 20th century various clinical features and pathophysiology was stemmed from karel Fredrick wenkebach(1864-1940),Gordon moe(1915-1989),Bernhord lown and maurits Allessie[4].

EPIDEMIOLOGY:

AF is the most common arrhythmia treated in practice , 33% of arrhythmia related admissions are due to AF. Atrial fibrillation has assuming

increasing importance as the global burden is ever increasing and it is the commonest arrhythmia.

Indeed Braunwald in his lecture referred to the "growing Epidemic" of AF[5].There is a 5 fold increase in cerebrovascular accident and 3 fold increase in cardiac failure[6],there by increased morbidity and mortality, by understanding the stroke risk and the CHA_2DS_2VASc Score helps us to decide about antithrombotic strategy. Rhythm versus Rate control continues to be controversial issue.

In our country there is no proper epidemiological data available on AF, but in recent times there is a data about Indian patients from RELY and REALIZE Studies(Indian patient cohort).IHRS-AF registry is the Largest study in indian population[7].

INCIDENCE AND PREVALENCE:

Incidence of AF is Age and Sex related, and ranges from 0.1% per year before the the age of 40 years to higher than 1.5% year in women and higher than 2% per year in men older than 80 years. Life time risk of developing AF is approximately 25% for individuals 40 years old.

In the western country prevalence of AF is 1.5-2% in general population, and the average age of presentation is 75-85 years, the annual incidence below 65 years is 3.1 in males and 1.9 in females per 100 person years[8] .From a recent population based study in patients older than65 years the

prevalence in females is 4.85% lesser than that of males 9.1%[9]. In Framingham heart study AF developed 1.5 times more in men than in women.

An Increase in obesity accounts for 60% of the age adjusted increase in AF Incidence.

Underestimation of incidence and prevalence of AF is due to absence of much symptoms and undersampling in patients with paroxysmal AF are more important constraints to the understanding the epidemiology of AF.

The first study conducted in India was in 1995 including 984 people, findings was only 0.1% of prevalence of AF, this low estimate is due to all were healthy persons and moreover they are subjected to only single ECG, and 6% of them were above 65 years old. Among Indians the west Birmingham study shows prevalence was 6%.

30% in Cardio vascular Health study and Stroke prevention in AF-111 study (SPAF-111) detected AF in 45% of persons incidently when they were subjected to ECG for other reasons.

A community based study shows age adjusted incidence of AF per 1000 person years increased between 1980 and 2000 from 4.4 to 5.4 in men and from 2.4 to 2.8 billion in women [10].

MORTALITY RELATIONSHIP:

AF is associated with twofold increase in the risk for all cause of mortality. Even in person who is not having clinically any cardiovascular disease AF still contributing to more mortality. “Framingham study” shows AF was independently increases the risk of Death in Males (OR: 1.5; with 95% CI : 1.2- 1.8) and Females (OR:1.9; 95% CI : 1.5 – 2.2).

INCIDENCE OF CEREBROVASCULAR ACCIDENT:

AF is associated with fivefold increase in risk for Stroke[11], overall this disorder contributing to 75000 strokes per year and it is the major cause of embolic stroke. Presence of other comorbid illnesses are also contributing factors for development of Stroke.

PATHOPHYSIOLOGY:

STRUCTURAL ALTERATIONS AND PATHOLOGICAL FEATURES:

Structural changes that alter the atrial architecture potentially leads to development of AF[12],changes include Inflammation, Hypertrophy and Fibrosis, occurs mostly due to underlying cardiac disease associated with coronary heart disease, valvular heart disease, hypertension, heart failure and cardiomyopathies, all these will lead to dilatation of atrium, altered wall stress, increased LA pressure. Likewise ischemia of atrium from CAD and diseases like hemochromatosis, amyloidosis, sarcoidosis also tends to promote AF.

Patients with paroxysmal AF without any underlying structural heart disorder biopsy from atrium revealed infiltrates of inflammation consistent with fibrosis and myocarditis[13].

Extracardiac conditions like systemic hypertension, obesity, obstructive sleep apnea syndrome, hyperthyroidism, alcohol, drugs, all of these have pathologic effects on the cellular function and structure of atrium.

Most common and frequent pathologic feature is Atrial fibrosis and atrial muscle mass loss, inter nodal tract muscle loss. Mild to moderate fibrosis occurs in AF of less duration, loss of muscle mass and fibrosis of severe in nature occurs in long standing AF.

Myocardial fibrosis is the feature of atrial fibrillation common to both human and experimental animal, atrium is very sensitive to profibrotic signalling pathways than that of ventricles because it contains large quantity of fibroblasts.

Rapid ventricular pacing in experimental animals produces atrial fibrosis thereby susceptible to AF, during atrial rapid pacing also fibrosis occurs. Prolonged rapid pacing of atrium increases susceptibility to AF, in persons having AF and animals subjected to pacing shows alteration in mitochondria, loss of myocyte from glycogen deposits and abnormal gap junction will lead to Apoptosis and cell necrosis[14].

Noninvasively late gadolinium enhancement MRI Imaging is used for identification and quantification of the fibrosis[15]. Studies also shows that fibrosis strongly correlated with the development of stroke[16],and also response to catheter ablation was decreased[15].

Atrial dilatation occurs due to systemic hypertension, coronary heart disease, dilated cardiomyopathy will leads to stretching of myocardium, which activates various molecular mechanisms includes Renin-Angiotensin-Aldosterone pathway, Angiotensin-II,TGF-β, these molecules or pathways induce inflammation and production of connective tissue growth factors and fibrosis so on.

Microscopic and macroscopic changes appears in the atrium begins in the first year of life. During 4^{th} to 5^{th} decades droplets of fats appears in the region of Atrio ventricular node and septum, these changes with ageing results in myocardial fibers loss and fatty deposition these things found in older persons.

Histologically Patchy fibrosis with juxtaposed normal atrium contributes to heterogeneity of atrial conduction.

Patient with Rheumatic Heart disease we can appreciate presence of Ascoff bodies pathognomonic of RHD, Anitschkow cells otherwise called as Caterpillar cells, Fish mouth appearance of valves are present.

MECHANISMS OF ATRIAL FIBRILLATION:

ELECTROPHYSIOLOGICAL MECHANISM:

There are lot of mechanisms which contributes to the development AF all mechanisms may coexist in an individual patient. Mechanisms involved in the development of AF and sustaining its course is more complex, Triggering events may differ from maintenance mechanisms. AF is more often initiated by small re-entrant or rapidly firing focus in the sleeves of atrial musculature along the pulmonary veins.

The clinical Phenotypes named paroxysmal, persistent and chronic AF have electrophysiologically different characteristics, because of remodeling and clinical modulators of different variety that affect the substrates such as atrial stretch, myocardial ischemia, cardiac failure, inflammation, fibrosis, sympathetic and parasympathetic influences.

There are two principle electrophysiological Mechanisms involved which are the reasons for development of fibrillatory activity. They are

1. Automatic one are more, triggered ,or foci of micro reentry called as Drivers, they are fires at rapid rates produces fibrillatory activity.

2. Multiple Re-entry circuits that meanders the entire atrium that annihilates and reforms wavelets which ultimately leads to accentuation of fibrillatoryactivity.

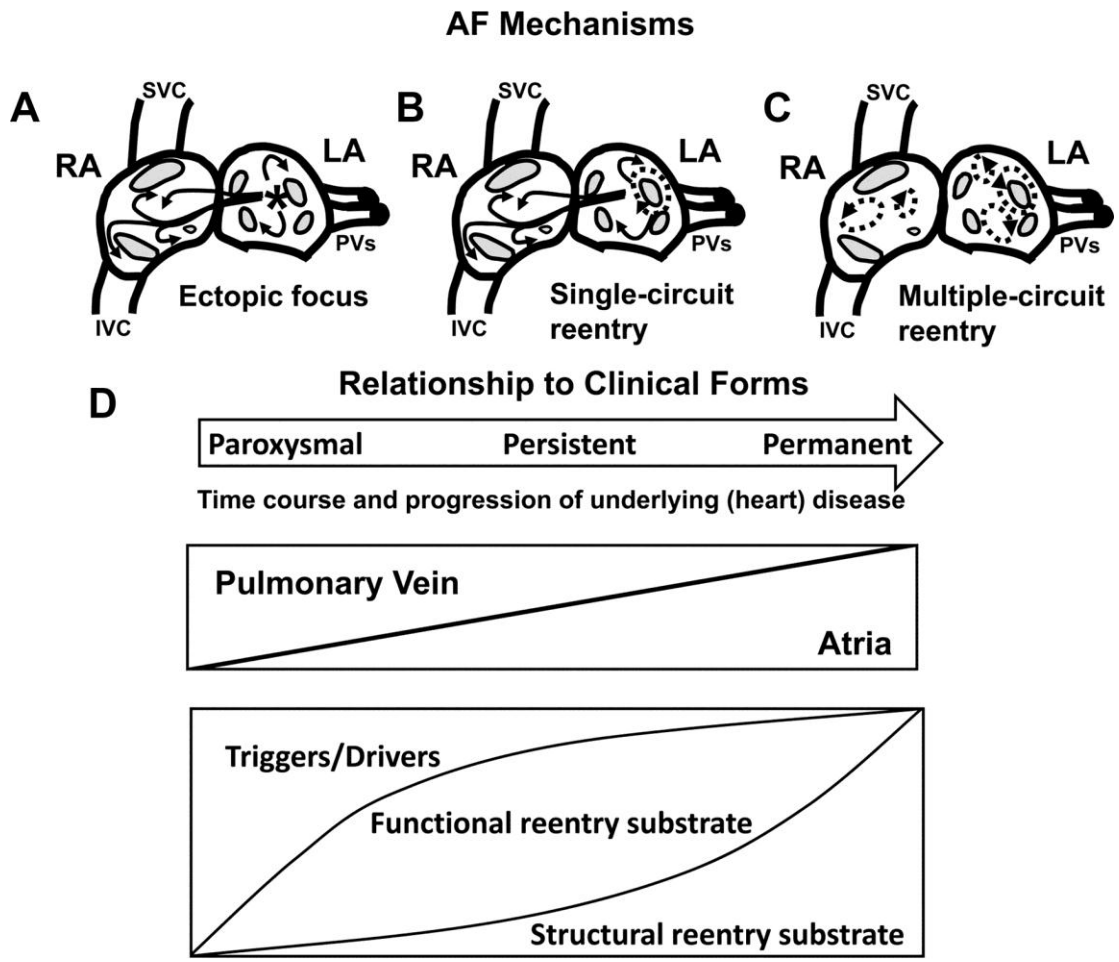


Figure1: Principal atrial fibrillation (AF)–maintaining mechanisms. **A**. Local ectopic firing, **B**. Single-circuit reentry, **C**.Multiple-circuit reentry, **D**. Clinical AF forms and relation to mechanisms.

Most of the times, these two mechanisms may be present simultaneously. Studies shows site of dominant frequency of discharge is in left atrium, with a left to right gradient.

One recent time study shows, by subjecting the patients to multiple electrocardiograms recorded simultaneuosly and with signal processing technique by obtaining computerized maps, reveals foci of fibrillatory sources

and electrical rotors. A mean of 2.1 sources was found in 97 % of 101 patients, of which 30% was Focal sources and 70% was Motor Rotors[17].

MECHANISM OF TRIGGERS IN AF:

Ectopic Focal discharges often Inciting event in the development AF[18]. Anatomical and electrophysiological specific characteristics of atriopulmonary vein junctions and pulmonary veins responsible for arrythmogenic propensity. In paroxysmal AF rapid foci of discharges often arises from sleeves of myocardium of LA that extending to pulmonary veins, this is the basis for the radio frequency catheter ablation by doing pulmonary vein isolation.

Re-entry occurs because of the conduction disturbances that will lead to relatively depolarized resting potentials in pulmonary vein myocytes, refractoriness in pulmonary veins and action potentials which are abbreviated also favours the development of re-entry[19]. Abnormal automaticity and trigger that also arise from isolated pulmonary vein myocytes.

Other sites for development of ectopic foci of discharges includes Coronary sinus, septum , venae cavae, posterior LA , Marshall Ligament.

There are other sources of abnormal activity producers present in pulmonary veins, which includes

1.Interstitial cells[20],

2. Melanocytes[21],

Event that Trigger delayed after depolarizations include intracellular calcium metabolism abnormality due to diastolic calcium leak from sarcoplasmic reticulum also plays an important role in the occurrence of AF[22].

COMPLEX FRACTIONATED ATRIAL ELECTROGRAMS:

In persistent type of AF atrial substrate changes including interstitial fibrosis which give rise to slow, anisotrophic and discontinuous conductions lead on to "complex fractionated atrial electrograms" and re-entry.

FACTORS RESPONSIBLE FOR MAINTENANCE OF AF:

The following theories gives explanation to the maintenance AF which includes

1.Rapidly firing foci of ≥ 1, which is responsible for activity from ganglion plexus present in the cardiac tissue.

2.Re-enterant wavelets of independent in nature, in multiple quantity associated with conduction and refractoriness of heterogenous nature.

3.Spiral wave Re-enterant circuits or, ≥ 1 Rotors[23].

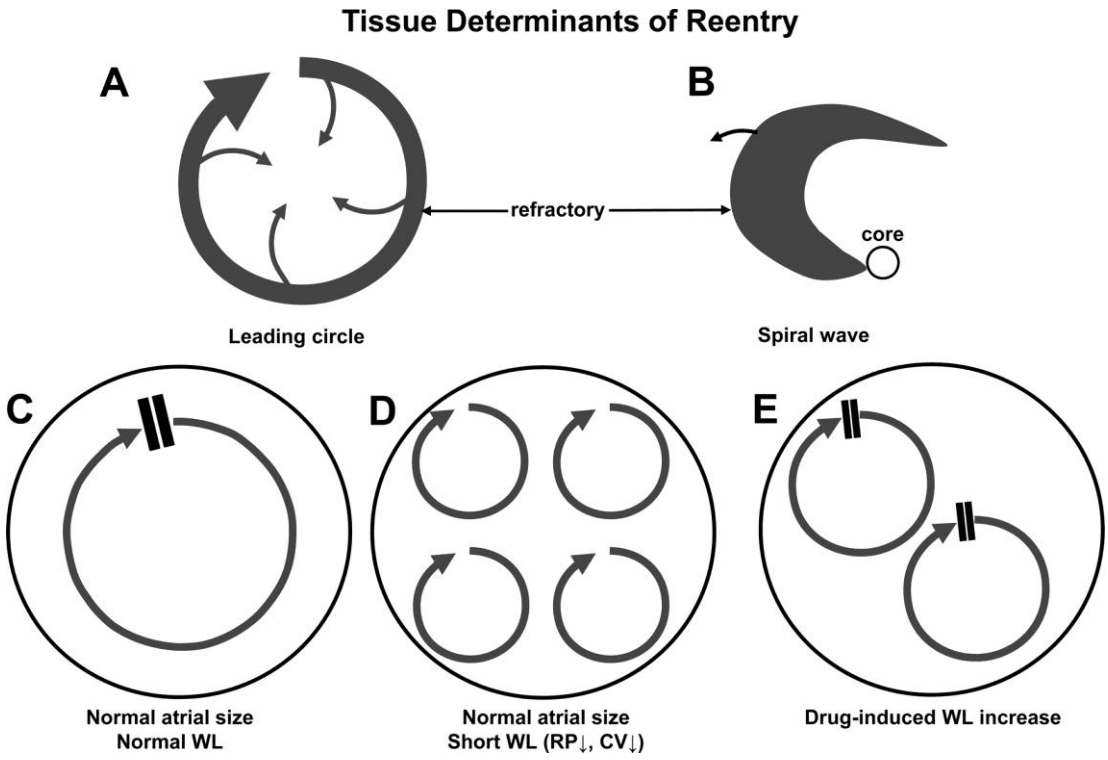


Figure 2: Models of re-entry and implications for atrial fibrillation (AF). **A**. Leading circle,**B**. Spiralwave re-entry, **C** to **E**, Role of wavelength(WL) in AF maintenance based on leading circle model, **C**. In normal atrium, the reentrant waves that can be accommodated is less, and re-entry easily terminates, **D**.When WL is reduced, by decreasing the refractory period (RP) or conduction velocity (CV), reentrant circuits are lesser and so much can be accommodated; self-termination is AF becomes unlikely, **E**. Drugs that increase WL lessens the number of circuits, leads to AF termination.

Rotor excitation with a single rapid focus, leads to refractory tissue and breakup of wave fronts during propagation, results in fibrillatory or irregularly irregular conduction[24].

Forementioned possible factors leads to the development of lot of Treatment strategies.

1.Ablation lines, maze procedure in atrium interrupts the pathways of Spiral re-rentry and multiple wavelets.

2.Rapid drivers (mean 2%) in less quantity were identified in a group of patients with different types of AF using Biatrial phase mapping[25].

3.Continuous biatrial mapping using non invasively gives different results. There is a role mostly for focal sites and multiple wavelets than Rotor Activity[26].

ROLE OF AUTONOMIC NERVOUS SYSTEM IN AF:

AF is provoked by parasympathetic and or sympathetic stimuli[27], parasympathetic and or sympathetic activation will leads to provoking of arrhythmias in atrium[28].

Activation of specific Pottasium current,$I_{K,Ach,}$ leads to shortened atrial action potential duration and refactoriness heterogeneously, increases the susceptibility to Re-entry. Sympathetic stimuli leads to increased intracellular calcium level which results in triggered activity and automaticity.

Near the pulmonary vein-LA junctions and the ligament of Marshall epicardial fat present, in which autonomic ganglionic plexus present, stimulation of this ganglia in experimental animals produces rapid atrial activity.

VAGALLY MEDIATED AF:

AF is occurs during conditions of high parasympathetic tone, such as following meals and during sleep, even in persons with structurally and physiologically normal heart called as "vagally mediated AF".

During exercise "stimulation of adrenergic system" also provokes a AF in some of the patients[29].

ATRIAL TACHYCARDIA REMODELING:

Progression from paroxysmal to persistent of AF occurs over a period of time, if AF duration is less than 6 months cardioversion of AF and maintaining in sinus rhythm will be successful[30].studies demonstrate that AF produces structural and electrical remodeling such that "AF begets AF" consistent with progressive nature of atrial fibrillation[31].

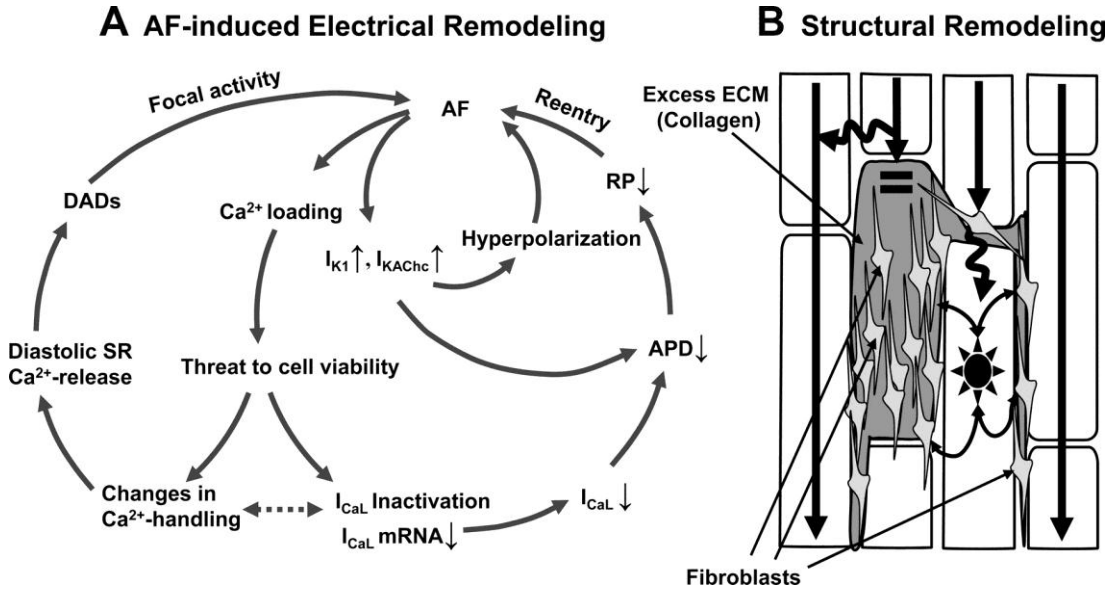


Figure 3: AF Types–promoting remodeling. Electric remodeling (**A**) is characterized by decreased in action potential duration (APD) because of AF

and increased delayed after depolarization (DAD) risk. Structural remodeling (**B**) involves death of cells, proliferation of fibroblast, and more extracellular matrix (ECM) production, causes fibrosis. Fibrosis will prevent electric propagation, favors re-entry. Interactions between Fibroblast-cardiomyocyte activates re-entry and ectopic impulse production. RP- refractory period; SR-sarcoplasmic reticulum.

RENIN ANGIOTENSIN ALDOSTERONE SYSTEM:

Electrophysiologic and structural changes in the atrium and ventricle increases the susceptibility to arrhythmia which are brought out by stimulation of renin-angiotensin-aldosterone system[32].The following are effects of this system which are responsible for production AF,

1.Hemodynamic adverse effects,

2.Increased intracellular calcium from activation of multiple cell signalling cascades,

3.Hypertrophy,

4.Apoptosis,

5.Oxidative stress,

6.Growth related factors that promote fibrosis,

7.Cytokine release and inflammation,

8.modulation of gap junction and ion channel dynamics.

If there is any variation occurs in the ACE gene expression plasma concentration of angiotensin-II will increase and thereby risk of AF formation elevated.

Likewise over expression of ACEs selectively results in dilatation of atrium, fibrosis and susceptibility to AF increased. During atrial tachypacing components of renin-angiotensin-aldosterone system synthesized in atrial myocardium are increased.

Aldosterone plays an important role in the causation of angiotensin-II mediated inflammation and fibrosis, incidence of AF is more in Patients with primary hyperaldosteronism.

Studies shows that in experimental models of heart failure, Eplerenone and Spiranolactone reduces both susceptibility to AF and atrial fibrosis, in this basis patients given with eplerenone are associated with decreased occurrence of AF in heart failure patients[33].

INFLAMMATION AND OXIDATIVE STRESS:

These mechanisms also plays an role in production of AF which includes,

1.Rise in plasma concentrations of C- reactive protein during inflammation (e.g.,associated with cardiac surgery and pericarditis) linked with development of AF[34].

2.Interleukin-6 and C-reactive protein increased in patients with AF, increased levels of C-reactive protein predicts the development of AF and also it predicts the relapse of AF after cardioversion.

3.Gene expression variation in the promoter region of interleukin-6,influences the development of AF in post operative patients.

4.Ageing,inflammation, activation of renin-angiotensin-aldosterone system, Environmental stress all will produce oxidative damage to atrium.

5.Because of oxidative damage upregulation of genes of reactive oxygen species are occurs these are responsible for oxidative changes in atrium of patients with AF.

6.Because of apparent contribution of NAD(P)H oxidase production of atrial superoxide increased in patients with AF and also in experimental animal models[35].In post operative patients given with antioxidant Ascorbate decreases the electrical remodeling and thereby decreased AF[36].

GENETIC FACTORS:

Research about genetic forms of AF have been under study for many years but incidence of this type of AF is very rare[37],population based studies suggest that AF is a heritable disease[38].

Family history of AF in a first degree relatives will independently increases AF risk 2 fold[38].

Polygenic inheritance is more common than monogenic inheritance in the causation of AF, ion channels are principally affected by monogenic inheritance[39].

Genetic linkage study identified the potentially pathogenic loci responsible for development of AF[40].

Multiple susceptibility signals are identified at chromosome 4q25 loci[41],they are responsible for expression of transcription factor PITX2 alteration of this is responsible for AF[42].

Familial AF is caused by several mutations, their role in causation have been studied and identified[43]. These mutations are,

1.Gain of function mutation that causes repolarization of pottasuim currents leads to shortened facilitation of atrial re-entry and and atrial refractoriness.

2.Multiple polymorphisms in the causation of AF is idiopathic, and they are associated with heart diseases having structural abnormality or occurs postoperatively in patients have been discovered[43].

3.Because of these polymorphisms genes responsible for sodium and potassium channels, connexin 40, interleukin-10, sarcolipin, renin-angiotensin-aldosterone system, endothelial nitric oxide synthase all are affected.

4.Ultimate results will includes changes in conduction, fibrosis, calcium handling which are the predisposing factors in the development of AF.

CAUSES OF ATRIAL FIBRILLATION:

There are so many causes or risk factors which produces the risk of AF which includes,

CARDIAC	**NON CARDIAC**
1. Systemic Hypertension,	Age
2.Ischemic heart disease,	Hyperthyroidism
3.Rheumatic mitral valve disease,	ExcessiveAlcoholintake
4.Hyprtrophic and dilated cardiomyopathy,	Chronic obstructive pulmonary disease
5.Congestive cardiac failure	-Obstructive sleep apnoea syndrome
6.Diastolic dysfunction and heart failure	-Diabetes mellitus
7.Pericarditis and Myocarditis,	-Obesity
8.Post cardiac surgery	-Pulmonary hypertension
9.Sick sinus syndrome,	- Pulmonary embolism
10.Atrial septal defect,	-Pneumonia
11.Restrictive cardiomypathy	- Drugs(e.g.,Theophylline)
12.Mitral valve prolapse syndrome	-Amyloidosis.
13.Increased pulse pressure	-Smoking
	-Exercise
	-Genetic
	-Familial
	-European Origin

REVERSIBLE OR TEMPORARY CAUSES[44,45]:-

1. Post cardiac or thoracic surgery
2. Myocardial infarction
3. Pericarditis and Myocarditis
4. Pneumonia
5. Pulmonary embolism
6. Holiday heart syndrome(Binge Alcohol intake)
7. Hyperthyroidism
8. Electrocution.

AF occurs because of Wolff-Parkinson-white (WPW) syndrome, atrial ectopic tachycardia, AV nodal re-enterant tachycardia resolve after catheter ablation therapies for these arrhythmias[46].

ELECTROCARDIOGRAPHIC RISK FACTORS:-

-Left ventricular hypertrophy

ECHOCARDIOGRAPHIC RISK FACTORS:-

-Left atrial enlargement

-Increased LV wall thickness

-Decreased LV fractional shortening

BIOMARKERS:-

-Increased brain natriuretic peptide

-Increased C-reactive protein

One study shows that 56% of the population-attributable risk of AF could be due to more than or equal to one risk factor[47].

Systemic hypertension:

Most of the patients with AF have systemic hypertension usually with left ventricular hypertrophy,14% of all cases of AF have systemic hypertension[48],apart from overt hypertension those patients with prehypertensive range and wide pulse pressure are also associated with risk of developing AF.

Coronary heart disease:

AF is a common complication of Acute coronary syndrome[49], prevalence of both obstructive and non obstructive CAD are more in patients with AF than patients without AF.

Valvular heart disease:

Valvular heart disease increase the risk of AF with 1.8 to 3.4 fold in men and women respectively[48],although any valve lesion can lead to AF left sided valvular heart disease particularly rheumatic heart disease has high prevalence,29% of isolated mitral stenosis,16% of isolated mitral regurgitation ,52% of coexisting mitral stenosis and regurgitation ,70% with mixed mitral and tricuspid regurgitation associated with AF[50].

In developing countries rheumatic heart disease is the most common cause of AF that too mitral stenosis is the most common cause of AF, and it is

more common in women than men[51],compared to western countries 15 -20 years earlier Indian patients with RHD develop AF[52].

Cardiomyopathy and Cardiac failure:

Hypertrophic cardiomyopathy has been associated with 10% to 28% AF cases[53].

Heart failure and AF often coexist, with increasing symptoms of heart failure AF prevalence will also be increased,<5% to 10% with NYHA class I,10% to 26% in NYHA class II-III,40% to 50% in NYHA class IV[54].Cardiac failure increases the risk of AF by 4.5 to 5.9 fold[48].Apart from systolic heart failure isolated diastolic heart failure also increases the incidence of AF[55].

Congenital heart disease:

In congenital heart diseases atrial tachyarrythmias present with more prevalence[56],and also they are the most common complication in adult patient with congenital heart disease. Among the congenital heart diseases particularly tetrology of fallot, atrial and atrioventricular septal defects, left sided obstructive heart diseases, Ebstein anomaly are associated with increased prevalence of AF ,in these conditions atrial macro re-enterant arrhythmias are the reasons for AF. In these lesions left sided hemodynamic changes act as important AF risk determinants[57].

Thyroid dysfunction:

Risk of AF strongly associated with thyroid dysfunction, increased risk of AF is associated though with overt hyperthyroidism(increased incidence of AF by 3 to 6 fold versus those with normal thyroid status),an apparently linear relationship has been studied between AF risk and thyroid function, with the increasing and decreasing levels of thyroid stimulating hormone, relative risk of 1.1 with euthyroid to 1.2 with subclinical hyperthyroid,to1.4 with subclinical hyperthyroid and suppressed TSH compared with normal thyroid status[58],it has been postulated that increased trigger activity and increased automaticity because of more β-adrenergic activity predisposes to AF.

Obesity:

Obesity and obstructive sleep apnoea syndrome both associated with each other and both increase the risk AF independently[59],increased systemic inflammatory response and dilatation of atrium are the causes of AF in obesity, for every unit increase in BMI, incident of AF increases by 3% to 7%[60].Hypoxia and autonomic tone surge, hypertension are the possible mechanisms in the development of AF in sleep apnoea syndrome.

Diabetes mellitus:

It has been associated with increased risk of by 1.4 to 1.6 fold, not only because of shared risk factor profiles (Diabetes associated with CAD, HF, OSA, autonomic dysfunction, and systemic inflammation),longer duration

of disease and poorly controlled glycemic control has been independently increases the risk AF[61].

Chronic kidney disease:

Prevalence of AF more with chronic kidney disease, even after accounting for common associated factors. Risk of AF increases with severity of AF(e.g.,with an eGFR of 30-59 and <30ml/min per 1.73 m^2,HR is 1.3-1.6 and 1.6-3.2 respectively),end stage renal disease is associated with increased incidence of AF, adjusted HR,1.67-1.77[62].

Physical activity and exercise:

Regular moderate physical activity gives beneficial effects on cardiovascular system and decrease the risk of AF, but excessive or vigorous sports activity are associated with higher prevalence of AF[63],in this group of population >3 episodes of AF paroxysms are likely to occur in vagal contexts(sleep, at rest, postprandial) compared with healthy people(57% Vs 18% in non high performance athletes)[64].

Alcohol:

Ethanol consumption and AF relationship has been known for several years, acute paroxysmal AF is associated with binge alcohol intake(Holiday Heart syndrome).

Though moderate intake of alcohol does not increase the risk of AF, heavy intake (≥ 36g/dl) increase the risk, it has been noted that consumption

and subsequent withdrawal from alcohol will results in impairment of vagal tone, hyper adrenergic tone, changes in conduction properties of atrium all are considered to be predisposes to AF[65].

Smoking:

Smoking has also been associated with risk of AF development, with more risk in those who are smoking(highest tertile ,> 675 cigarette-years)[66],AF recurrence after catheter ablation is associated with continuous tobacco use[67].

CLINICAL FEATURES

SYMPTOMS:

Symptoms of AF varies between patients and it ranges from nil symptoms to severe disabling status.

The most common symptoms are,

1. palpitation,
2. fatigue,
3. shortness of breath,
4. chest pain,
5. syncope,

Other less common symptoms are

1. effort in tolerance,
2. fluttering or thumping in the chest,
3. dizziness,
4. confusion
5. weakness
6. reduced ability to exercise
7. abdominal pain

Patients with paroxysmal AF symptomatic mostly, but sometimes they presents with asymptomatic episodes.25% of the patients approximately asymptomatic and they are mostly patients with persistent AF and elderly patients.

Uncommon symptom of AF is syncope, in sick sinus syndrome it can be caused by long sinus pause on termination of AF, in a AF patients with rapid ventricular rate syncope occurs because of either severe drop in blood pressure or because of vasodepressor (neurocardiogenic)syncope that is due to tachycardia induced trigger.

SIGNS:

1. Hallmark of AF is an irregularly irregular pulse,
2. Pulse deficit : Because of short R-R intervals adequate time for left ventricular filling not available, results in a low stroke volume and absent peripheral pulse, leads to a ”pulse deficit”, in which compared to apical rate peripheral pulse slower.
3. Jugular venous pulsations will be irregular
4. “First heart sound” is variable.
5. Absence of “fourth heart sound” which is heard during sinus rhythm.
6. Findings of associated valvular heart disease or myocardial infarction .

CLASSIFICATION OF AF:

They are classified based on the duration of episodes of AF using “simplified scheme revised from the 2006 AF Full revision guideline”[27].

The following are the techniques were used to classify AF, Pacemakers, Implanted loop recorders, Defibrillators, by using them we can describe the,

1. Rate
2. Frequency
3. Duration of abnormal atrial rhythms

CLASSIFICATION:

1. Paroxysmal,
2. Persistent,
3. Long standing persistent
4. Permanent,
5. Non valvular

Table given below has useful clinical relevance, that is we can predict the outcomes of treatment, such as catheter ablation, that is better for paroxysmal AF than persistent AF[27],even after restoring to sinus rhythm by cardioversion, the duration of the episode(s) of AF is not known, in some patients both paroxysmal and persistent AF can occur together

Term	Definition
Paroxysmal AF	• AF that terminates spontaneously or with intervention within 7 d of onset. • Episodes may recur with variable frequency.
Persistent AF	• Continuous AF that is sustained >7 d.
Longstanding persistent AF	• Continuous AF of >12 mo duration.
Permanent AF	• Permanent AF is used when there has been a joint decision by the patient and clinician to cease further attempts to restore and/or maintain sinus rhythm. • Acceptance of AF represents a therapeutic attitude on the part of the patient and clinician rather than an inherent pathophysiological attribute of the AF. • Acceptance of AF may change as symptoms, the efficacy of therapeutic interventions, and patient and clinician preferences evolve.
Nonvalvular AF	• AF in the absence of rheumatic mitral stenosis, a mechanical or bioprosthetic heart valve, or mitral valve repair.

"Lone or undetermined AF" is AF occurring in an individuals < 60 years without any structural heart diseases or hypertension.

COMPLICATIONS:-

Some patients because of minimal symptoms or asymptomatic they don't seek medical advice and their initial presentation itself presented with stroke or thromboembolic complications.

1.Heart failure:

At rest approximately 20% of left ventricular stoke volume is by atrial contraction it will be lost in AF, and moreover it will cause LV dysfunction and irregular rhythm of ventricles[68].AF decompensates ventricular function, increased prevalence of AF found in congestive cardiac failure.

2.Determinants of Thromboembolism:

Most important complication of AF is thromboembolism and it is implicated in the causation stroke in elderly, the following Figure depicts the formation of thromboembolism.

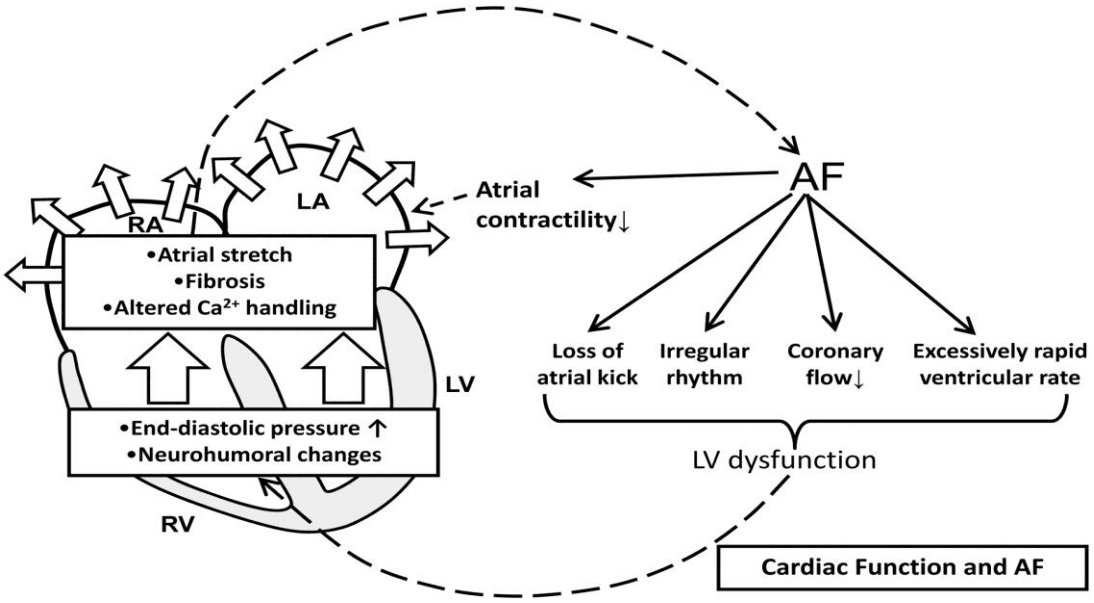


Figure 4. :During AF Dynamic interactions between atrial and ventricular function .

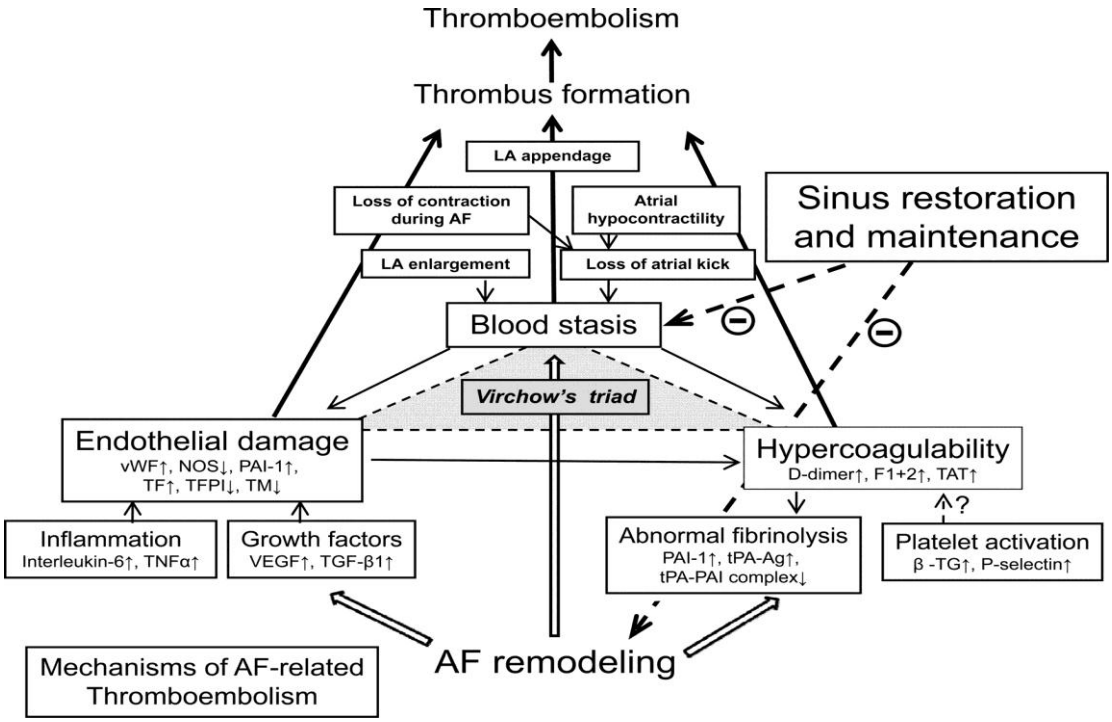


Figure.5 :Mechanism of AF related thromboembolism. **vWF**- von Willebrand factor;**NOS**-nitric oxide synthase;**TF**-tissue factor;**TFPI**-tissue factor pathway inhibitor.**TM**-thrombomodulin;**TNF**-tumor necrosis factor-α;**VEGF**-vascular endothelial growth factor;**TGF**-β1-transforming growth factor-β1;**F1+2-**

prothrombin fragment 1+2;**TAT**-thrombin/antithrombin complex;**tPA-Ag**-tissue-type plasminogen activator–antigen; **tPA-PAI**-tissue-type plasminogen activator/plasminogen activator inhibitor; **β-TG**- β-thromboglobulin.

3.Stroke:

The most common complication in AF is thromboembolism indued stroke, AF is associated with 5 fold increased risk of stroke.In a prospective study, subclinical atrial tachyarrythmias(atrial rate>190 beats /min for 6 minutes) were detected by device interrogation, subclinical atrial tachyarrythmias was independently associated with increased risk of stroke.

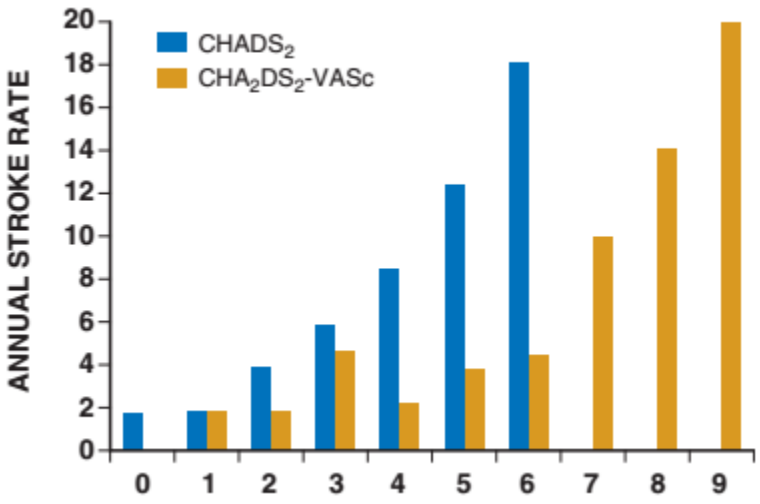


Figure 6. Annual risk for stroke (percent risk per year) based on the $CHADS_2$ and CHA_2DS_2-VASc scores. (Based on data from Lip GY: Implications of the CHA_2DS_2-VASc and HAS-BLED scores for thromboprophylaxis in atrial fbrillation. Am J Med 124:111, 2011.

DIAGNOSTIC EVALUATION

Initial diagnostic evaluation of AF includes,

A)Minimum evaluation,

B)Additional investigations, which all depends upon the presentation of patients clinical situation.

A) Minimum :

1. Patient's clinical history and physical examination findings,
2. ECG,
3. Chest X-ray,
4. Transthoracic Echocardiography,
5. Blood investigations,

B) Additional investigations:

1. 6- minutes walk test
2. Exercise testing
3. Holter or event monitoring
4. Transesophageal echocardiography(TEE)
5. Electrophysiological study.

A) 1.Clinical history and physical examination:

Here we have to assess the following things,

a) Nature of the symptomatology

b) Clinical types of AF(paroxysmal, persistent, permanent)

c) Onset of first episode or day of detection

d) Frequency, duration, aggravating factors, modes of initiation and termination of AF

e) Response to any drugs administered

f) Presence of underlying heart diseases or any reversible conditions

A) 2. Electrocardiogram(ECG):

ECG is the important and essential tool for establishing and confirming the diagnosis of AF, the following are the ECG finding of AF,

a) Very irregular and disorganized atrial activity represented as fibrillatory waves called as 'F' waves.

b) 'F' waves may be fine or coarse with varied morphology mistaken for P waves

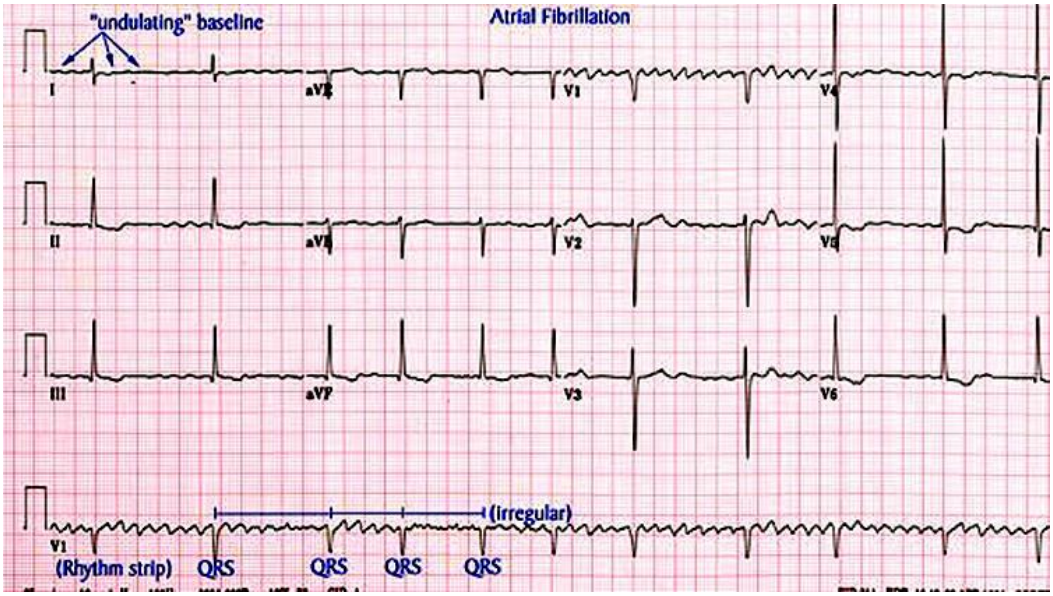
c) Instead of 'F' waves ,a flat line with irregular R-R intervals may be present.

d) Absent or no distinct P waves.

e) Atrial rate in AF is ≥350 beats/ minute

f) Ventricular rate is irregularly irregular and it is depends upon number of atrial impulses reaching atrioventricular(AV) node

g) Narrow QRS complex unless there is aberrant conduction, preexcitation or bundle branch block.



ECG is used to identify other features in a AF patient to find out other contributing or causative disease,

a) Rhythm to verify AF
b) Morphology and duration of ‘P’waves or ‘F’ waves.
c) Bundle branch block, preexcitation
d) Previous MI,
e) Other atrial arrhythmias
f) In patients who are taking anti arrhythmic therapy, to measure and follow, R-R intervals, QRS complex, QT intervals.

A)3.Chest X-ray:

Chest radiograph is done to find out any suspected pulmonary pathology contributing to AF ,to detect suspected cardiac failure, to see any cardiac chamber enlargement.

A)4.Transthoracic Echocardiography(TTE):

Echocardiography plays a important role in management and risk stratification of patients with AF. Echocardiography has also become an crucial part in the guidelines for management of patients with AF, especially in explaining the mechanisms of systemic thromboembolism in AF.

Transthoracic echocardiography(TTE) allows comprehensive and rapid assessment of cardiac anatomical structure and function. TTE is necessary for the initial evaluation of patient with fist episodes of AF, and gives clues to find out the etiology of AF, and helps the clinicians to start and alter the treatment approach. There are lot of studies shows that it will assist the clinicians in a difficult situation to take decision about antithrombotic prophylaxis. The following can be assessed by TTE,

1. Valvular heart disease
2. LA and RA size
3. LV and RV size and function
4. Left ventricular hypertrophy
5. LA thrombus(low sensitivity)
6. Pericardial disease.

Left ventricular systolic dysfunction shown via TTE in patients with atrial fibrillation, independently predicts the risk of stroke(relative risk 2.5;p<.001)[69].

LA size is useful predictor of recurrent AF, large LA size is associated with increased risk of developing AF[70],if LA size exceeds >4.5Cm^2 cardioversion is unlikely to be effective[71], LA size >4.0 Cm^2 is a single most strong predictor of increased risk of embolization[72],even in the absence of other causes for increased atrial size, atria increases with time in patients of AF[73].

Chronic duration of AF, increased muscle mass, left ventricular dilataion, annular calcification, mitral regurgitation, hypertension are independently predicts the LA size. Data from the Framingham study shows that 39% increased risk for subsequent development of AF, if LA dimension increase by 5-mm[74].

TTE is also a assess the atrial function, reduced both LA compliance and volume has been noted with the onset of AF and it also reduces cardiac function ,and risk of thromboembolism will be increased.

In patients with sinus rhythm, Presence of severe LV diastolic failure are associated with an increased risk for AF and heart failure, as assessed by TTE.

Septal thickness(IVSD) and left ventricular posterior wall thickness(LVPWD) are independent predictors of AF.

A)5.Blood investigations:

Includes Thyroid function test, Liver Function test, Renal function test done in the patients with first episodes of AF, and in those patients in whom ventricular rate is difficult to control with treatment.

B).Additional investigations:

One are more of the following investigations may be required depending upon the clinical situations.

1. 6-min walk test	• If the adequacy of rate control is in question
2. Exercise testing	• If the adequacy of rate control is in question
	• To reproduce exercise-induced AF
	• To exclude ischemia before treatment of selected patients with a type IC antiarrhythmic drug
3. Holter or event monitoring	• If diagnosis of the type of arrhythmia is in question
	• As a means of evaluating rate control
4. TEE	• To identify LA thrombus (in the LAA)
	• To guide cardioversion
5. Electrophysiological study	• To clarify the mechanism of wide-QRS-complex tachycardia
	• To identify a predisposing arrhythmia such as atrial flutter or paroxysmal supraventricular tachycardia
	• To seek sites for curative AF ablation or AV conduction block/modification

TREATMENT

A)Acute management:

1. New onset AF : patients with hypotension, angina, pulmonary edema treated with electrical cardioversion, after termination if again AF occurs ibutilide and repeat cardioversion should be given.

2. Acute rate control can be achieved with beta blockers ,calcium channel blockers such as oral or i.v verapamil and diltiazem, Digoxin is added in patient with cardiac failure.

B) Long term management of atrial fibrillation:

1.Pharmacological rate control:

According to ACC/AHA guidelines the following table describe about the pharmacological rate control measures.

CLASS	INDICATION
Class I (indicated)	Measurement of the heart rate at rest and control of the rate with pharmacologic agents (in most cases either a beta blocker or nondihydropyridine calcium channel antagonist) are recommended for patients with persistent or permanent AF In the absence of preexcitation, intravenous administration of beta blockers (esmolol, metoprolol, or propranolol) or nondihydropyridine calcium channel antagonists (verapamil, diltiazem) is recommended to slow the ventricular response to AF in the acute setting, with caution being exercised in patients with hypotension or heart failure Intravenous administration of digoxin or amiodarone is recommended to control the heart rate in patients with AF and heart failure who do not have an accessory pathway In patients who experience symptoms related to AF during activity, the adequacy of heart rate control should be assessed during exercise, with pharmacologic treatment being adjusted as necessary to keep the rate in the physiologic range Digoxin is effective after oral administration to control the heart rate at rest in patients with AF and is indicated for patients with heart failure or left ventricular dysfunction and for sedentary individuals
Class IIa (reasonable)	A combination of digoxin and either a beta blocker or nondihydropyridine calcium channel antagonist is reasonable to control the heart rate both at rest and during exercise in patients with AF. The choice of medication should be individualized and the dose modulated to avoid bradycardia It is reasonable to use ablation of the AV node or accessory pathway to control the heart rate when pharmacologic therapy is insufficient or associated with side effects Intravenous amiodarone can be useful to control heart rate in patients with AF when other measures are unsuccessful or contraindicated When electrical cardioversion is not necessary in patients with AF and an accessory pathway, intravenous procainamide or ibutilide is a reasonable alternative
Class IIb (may be considered)	When the ventricular rate cannot be adequately controlled both at rest and during exercise in patients with AF by a beta blocker, nondihydropyridine calcium channel antagonist, or digoxin, alone or in combination, oral amiodarone may be administered to control the heart rate Intravenous procainamide, disopyramide, ibutilide, or amiodarone may be considered for hemodynamically stable patients with AF involving conduction over an accessory pathway When the rate cannot be controlled with pharmacologic agents or tachycardia-mediated cardiomyopathy is suspected, catheter-directed ablation of the AV node may be considered in patients with AF to control the heart rate
Class III (not indicated)	Strict rate control (<80 beats/min at rest or <110 beats/min during a 6-minute walk) is not more beneficial than a resting rate of <110 beats/min in asymptomatic patients with persistent AF and an ejection fraction >40%, although uncontrolled tachycardia can lead to reversible left ventricular dysfunction over time Digitalis should not be used as the sole agent to control the rate of ventricular response in patients with paroxysmal AF Catheter ablation of the AV node should not be attempted without a prior trial of medication to control the ventricular rate in patients with AF In patients with decompensated heart failure and AF, intravenous administration of a nondihydropyridine calcium channel antagonist may exacerbate the hemodynamic compromise and is not recommended Intravenous administration of digitalis glycosides or nondihydropyridine calcium channel antagonists to patients with AF and a preexcitation syndrome may paradoxically accelerate the ventricular response and is not recommended

2.Rhythm control:

a)Cardioversion

First line drugs recommended for chemical cardioversion includes the follwing drugs,

1. Flecainide,
2. Dofetilide ,
3. Propafenone ,
4. Ibutilide .

b)Direct – current (DC) cardioversion;

Recommended when the ventricular rate is rapid and does not respond quickly to drug therapy in patients with

1. Ischemic heart disease,
2. Hypotension,
3. Cardiac failure,
4. WPW syndrome,
5. Rapid ventricular rate,
6. Patients with hemodynamic instability.

c)Maintenance of sinus rhythm:

According to ACC/AHA guidelines the following table describe about the maintenance of sinus rhythm measures.

CLASS	INDICATION
Class I (indicated)	Before initiation of antiarrhythmic drug therapy, treatment of precipitating or reversible causes of AF is recommended Catheter ablation by an experienced operator is useful in selected patients with symptomatic paroxysmal AF who have failed treatment with an antiarrhythmic drug and have a normal or mildly dilated left atrium and normal or mildly reduced left ventricular function
Class IIa (reasonable)	Pharmacologic therapy can be useful in patients with AF to maintain sinus rhythm and to prevent tachycardia-induced cardiomyopathy Infrequent, well-tolerated recurrence of AF is reasonable as a successful outcome of antiarrhythmic drug therapy Outpatient initiation of antiarrhythmic drug therapy is reasonable in patients with AF who have no associated heart disease when the agent is well tolerated In patients with lone AF without structural heart disease, initiation of propafenone or flecainide can be beneficial on an outpatient basis in patients with paroxysmal AF who are in sinus rhythm at the time of drug initiation Sotalol can be beneficial in outpatients in sinus rhythm with little or no heart disease who are prone to paroxysmal AF if the baseline uncorrected QT interval is shorter than 460 msec, serum electrolyte values are normal, and risk factors associated with class III drug–related proarrhythmia are not present Catheter ablation is a reasonable option for the treatment of symptomatic persistent AF
Class IIb (may be considered)	Catheter ablation may be reasonable for patients with symptomatic paroxysmal AF and significant left atrial dilation or significant left ventricular dysfunction
Class III (not indicated)	Antiarrhythmic therapy with a particular drug is not recommended for maintenance of sinus rhythm in patients with AF who have well-defined risk factors for proarrhythmia with that agent Pharmacologic therapy is not recommended for maintenance of sinus rhythm in patients with advanced sinus node disease or AV node dysfunction unless they have a functioning electronic cardiac pacemaker

B)Special situations:

1. Post operative Atrial fibrillation: Prophylactic treatment with beta blocker to prevent post operative AF in patients planned for cardiac surgery .
2. Acute Myocardial Infarction: Electrical cardioversion is recommended for patients with hemodynamic compromises or ongoing inchemias or when drugs failed to control the rate.
3. AF in WPW syndrome : Catheter ablation of the accessory pathway is recommended for patients With symptomatic AF in WPW syndrome.
4. Hyperthyroidisim: Beta blockers are the first line drugs for rate control in thyrotoxicosis patients with AF.

5. Hypertrophic Cardiomyopathy : The drugs used preferably either disopyramide with beta blocker , verapamil, or diltiazem or amiodarone for rate control.
6. AF during Pregnancy: Recommended drugs are digoxin , beta blocker or a nondihydropyridine calcium channel antagonist for rate control. DC cardio version is recommended in hemodynamically unstable patients.
7. Pulmonary Disease : Verapamil or diltiazem is used for rate control in patient with COPD.

C) Prevention of Thromboembolic Complications:

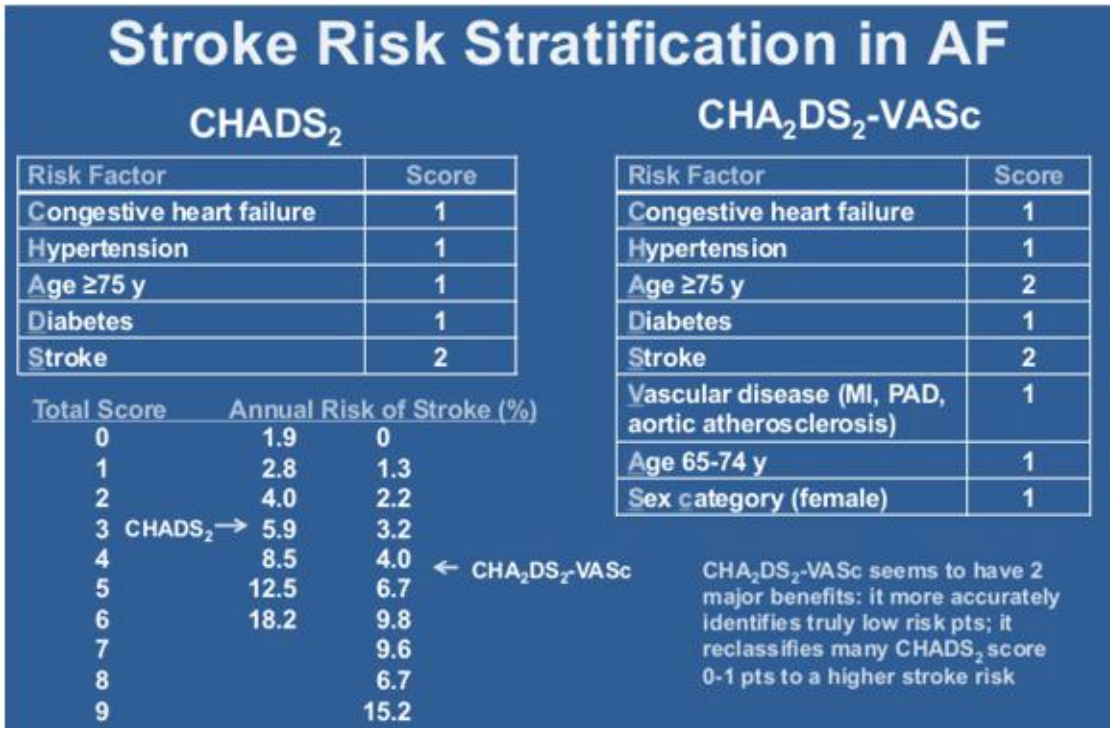
The main aim of treatment in patients with AF is to prevent thromboembolic complications such as stroke. There are two scoring systems have developed for 'risk stratification' they are as follows,

1.$CHADS_2$ scoring system:

A simple method to "risk stratify" patients is based on "$CHADS_2$ score" By using this scoring system we can predict the direct relationship between $CHADS_2$ score and the annual risk of stroke in patients with AF in the absence of warfarin or aspirin treatment, this score is very simple and it has predictive value.

2.CHA_2DS_2-VASc scoring system:

But recent studies have shown that "CHA_2DS_2–VASc score" more accurately differentiates low risk from intermediate risk patients.



Based on the scores the therapies are recommended as follows,

1. Aspirin is used prophylatically when " CHA_2DS_2–VASc score" of 0.
2. Aspirin for stroke prevention is recommended for patient with ' $CHADS_2$ score'of 0 .
3. Aspirin and or oral anticoagulant ,When the $CHADS_2$ score is 1.
4. Newer Anticoagulants: Dabigatran ,Rivaroxaban and apixaban for patients with AF in whom maintenance of therapeutic INR during treatment with warfarin is difficult.
5. Low molecular heparin is an alternative to unfractionated heparin for initiation of anticoagulation with warfarin.
6. Surgical removal or closure of LA appendage.

"HAS –BLED scoring system" was developed to risk stratify patients susceptible for bleeding complications. As the score increases from 0 to maximum of 9, there is a gradual increase in bleeding in patients treated with warfarin.

Letter	Clinical characteristic	Points awarded
H	Hypertension	1
A	Abnormal renal and liver function (1 point each)	1 or 2
S	Stroke	1
B	Bleeding	1
L	Labile INRs	1
E	Elderly (e.g. age >65 years)	1
D	Drugs or alcohol (1 point each)	1 or 2
		Maximum 9 points

D) Non pharmacologic management of AF:

The following are the non pharmacological options available for management of AF,

1. Pacing,
2. Catheter ablation,
3. Surgical removal or closure of LA appendage,
4. Maze procedure.

MATERIALS AND METHODS

Study design:- Cross-sectional study

Study period:- 6 months(April 2016 – September 2016)

Study area :- Govt. Kilpauk Medical College and Hospital, Chennai.

Study population:- Patients with New onset Atrial Fibrillation(in patients and out patients) in Department of General medicine and Department of Cardiology, Govt. Kilpauk Medical College and Hospital, Chennai.

Sample Size:- Was calculated based on 91% of AF having RHD as predisposing factor, α level 5%[95% confidence interval],absolute accuracy at 9%, so by calculating by this sample size is 50.since inflow of patients with AF to our hospital is very high, I have taken up sample size as 100 to my study.

Ethical clearance:- Ethics committee clearance was obtained.

Consent:- Informed consent obtained from all subjects for clinical examination and for doing investigations. Patient confidentiality maintained.

Inclusion criteria:- Patients aged more than 18yrs, Patients with clinically and electrocardiographically proven atrial fibrillation and hemodynamically stable patients.

Exclusion criteria:- Patients with atrial arrythmias other than atrial fibrillation and hemodynamically unstable patients.

Methodolgy:

100 patients with Atrial fibrillation were analysed in this study, and their general and clinical data was included in the proforma.

Patient's age, sex, clinical symptoms and past history of Systemic Hypertension, Rheumatic heart disease, Coronary Artery Disease, chronic obstructive pulmonary disease, Hyperthyroidism, Cardiomyopathy, Congenital heart disease, Stroke, and treatment history, were taken in to account.

Diagnosis of atrial fibrillation was done by absent P waves, fibrillatory (F) waves, irregularly irregular ventricular rate in ECG were taken as the evidence for AF.

Evaluation regarding etiology of AF is done by using ECG and Transthoracic echocardiogram, Chest radiograph were done in all patients.

For the history of Rheumatic heart disease H/O Rheumatic fever in the past with, migratory joint pain with no residual deformity were included, and confirmed by ECHO.

Diagnosis of Systemic hypertension was made by blood pressure with systolic BP > 140 mmHG and /or Diastolic BP > 90mmHG.

Presence of 'T' wave inversion and Significant Q waves in ECG, Regional wall motion abnormality in ECHO were taken as evidences for coronary artery disease.

COPD was diagnosed by using history of chronic cough and history of smoking, Chest radiograph, ECG, Transthoracic ECHO.

Thyroid Function tests were done only for 'at risk' cases and those who are presenting with signs and symptoms of hyperthyroidism. History of smoking and Alcohol were asked in all patients.

Clinical examination:

1. General examination
2. Vitals:-
    a) Pulse rate,
    b) Pulse deficit,
    c) Blood pressure,
3. Systemic examination,
4. Signs of hyperthyroidism,

Laboratory data:-

1. Conventional 12 lead ECG with rhythm strip,
2. Transthoracic echocardiographic examination,
3. Complete blood count,

4.Renal function test

5. Lipid profile Blood glucose levels-fasting and post prandial,

6. Chest Radiograph,

7. Thyroid function tests in selected patients,

In our study ,All patients were analyzed with 2D ECHO, M MODE and Color Doppler to find out the coronary heart diseases, if structural heart disease like congenital heart diseases, hypertensive heart disease, and dilated cardiomyopathies, hypertrophic cardiomyopathy.

Transthoracic echocardiographic assessment also includes the search for the presence of left atrial clot.

Transthoracic echocardiography (TTE) was done in all patients and the following parameters were assessed.

1. LVIDd(cm)

2. Ejection fraction%

3. IVSd(cm)

4. LVPWDd(cm)

5.RWMA

6.Valvular lesions

7.RA and LA Size(cm)

8.LA Clot

9.RV systolic dysfunction

Analysis of Data:

1. The different presentations of AF will be provided as % with 95% confidence interval.

2. The different predisposing factors will be provided as %.

3. The different parameters of Transthoracic Echocardiography will be provided in %.

The collected data were analysed with IBM.SPSS statistics software 23.0 Version.To describe about the data descriptive statistics frequency analysis, percentage analysis were used for categorical variables and the mean & S.D were used for continuous variables. To find the significant difference between the bivariate samples in Independent groups the Unpaired sample t-test was used.To find the significance in categorical data Chi-Square test and Fisher's Exact was used. In all the above statistical tools the probability value <.05 is considered as significant level.

DATA ANALYSIS

1.Baseline characteristics:-

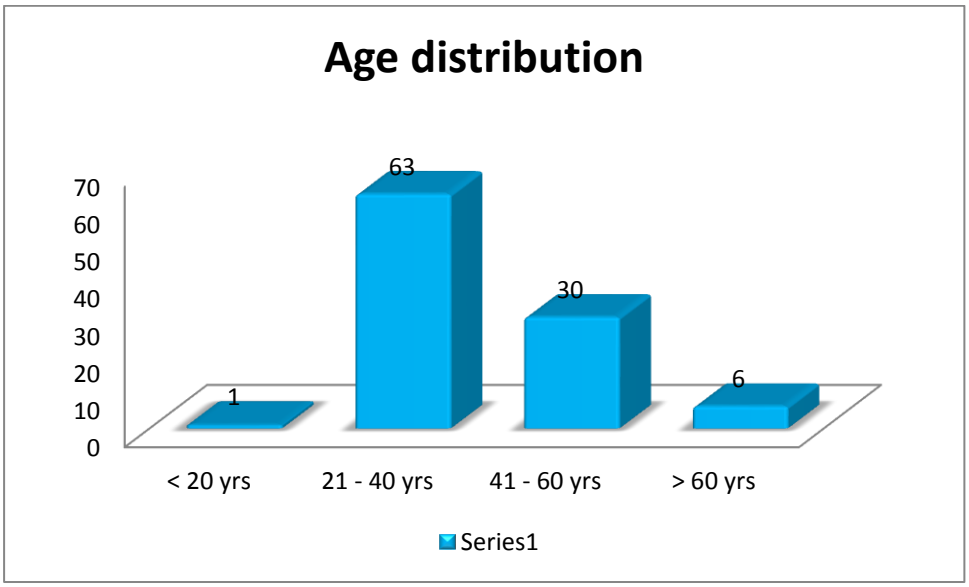
S.no	Total Number of cases	100
1.	Mean age in years	RHD; 35.92,NON RHD;51.70
2.	Males	32
3.	Females	68
4.	Systemic hypertension	7
5.	Rheumatic heart disease	77
6.	Coronary heart disease	4
7.	Chronic obstructive pulmonary disease	1
8.	Hyperthyroidism	2
9.	Hypertrophic cardiomyopathy	1
10.	Atrial septal defect	1
11.	Mitral valve prolapse syndrome	1
12.	Dilated cardiomyopathy	2
13.	Drug induced	1
14.	Lone or Undetermined AF	3

In our study 100 patients with AF were included, the mean age of our study population for RHD 35.92,Non RHD 51.70.

In our study females were more in number than males. Out of 100 total patients 68 were females,32 were males. In our study the number of patients with RHD were 77,and the remaining 23 cases had Non RHD etiological factors.

2.Age Distribution:

Figure 1.Showing Age Distribution



In our study we divided the patients into 4 Age groups, as follows

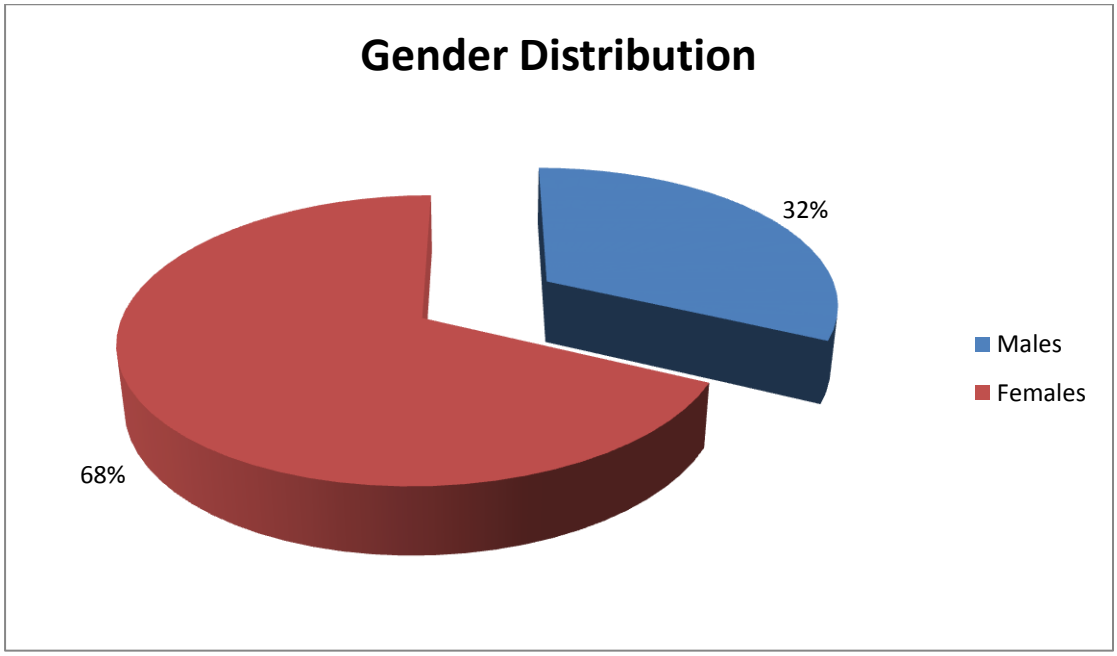
1. < 20 years – 1
2. 21-40 years – 63
3. 41-60 years – 30
4. > 60 years – 6

In our study maximum number of patients were in the 21- 40 years age group, and less than 20 years only 1patient is present,> 60 years there were 6 patients present.

3.Gender Distribution:-

In our study females were more in number than males. Out of 100 total patients 68 were females,32 were males .

Figure 2.Gender Distribution



4.Symptom Analysis:-

S.no	Symptoms	Prevalence
1.	**Shortness of breath**	66%
2.	**Chest pain**	35%
3.	**palpitation**	72%
4.	**syncope**	6%
5.	**fatigue**	28%
6.	**Limb weakness**	1%

			ETIOLOGY		
			Non RHD	RHD	Total
SYMPTOMS	1.	Count	2	9	11
		% within RHD	8.7%	11.7%	11.0%
	1+2	Count	2	5	7
		% within RHD	8.7%	6.5%	7.0%
	1+2+3	Count	1	3	4
		% within RHD	4.3%	3.9%	4.0%
	1+2+3+4	Count	0	1	1
		% within RHD	0.0%	1.3%	1.0%
	1+2+3+4+5	Count	0	1	1
		% within RHD	0.0%	1.3%	1.0%
	1+2+3+5	Count	1	5	6
		% within RHD	4.3%	6.5%	6.0%
	1+2+4	Count	0	1	1
		% within RHD	0.0%	1.3%	1.0%
	1+2+4+5	Count	0	1	1
		% within RHD	0.0%	1.3%	1.0%
	1+2+5	Count	0	4	4
		% within RHD	0.0%	5.2%	4.0%
	1+3	Count	6	15	21
		% within RHD	26.1%	19.5%	21.0%
	1+3+5	Count	1	1	2
		% within RHD	4.3%	1.3%	2.0%
	1+4+5	Count	0	1	1
		% within RHD	0.0%	1.3%	1.0%
	1+5	Count	0	4	4
		% within RHD	0.0%	5.2%	4.0%
	2.	Count	3	2	5
		% within RHD	13.0%	2.6%	5.0%
	2+3	Count	1	3	4
		% within RHD	4.3%	3.9%	4.0%
	2+5	Count	0	1	1
		% within RHD	0.0%	1.3%	1.0%
	3.	Count	6	8	14
		% within RHD	26.1%	10.4%	14.0%
	3+5	Count	0	6	6
		% within RHD	0.0%	7.8%	6.0%
	5.	Count	0	3	3
		% within RHD	0.0%	3.9%	3.0%

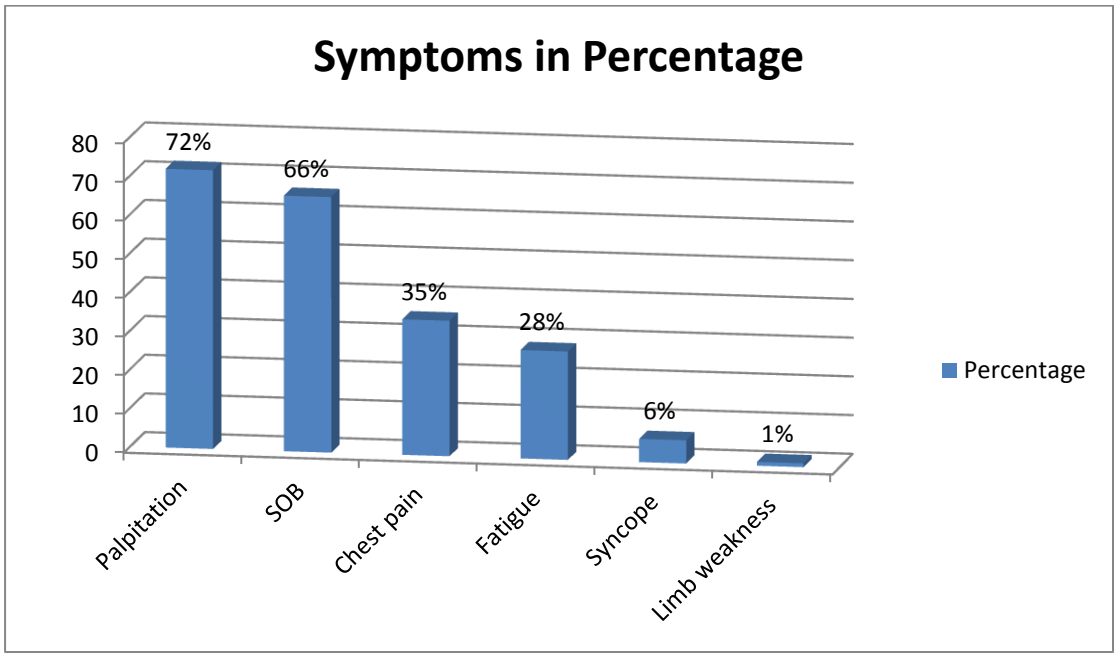
SOB -1; Chest pain -2; Palpitation -3; Syncope -4; Fatigue-5 ;Limb weakness-6

In our study predominant symptom was palpitation, which was present in about 72%,next comes shortness of breath which was present in about 66%,syncope accounted for 28%,and limb weakness was present in only about 1%.Many patients actually had multiple symptoms.

For the overall symptom analysis, we assigned a number for each symptom (SOB-1,Chest pain- 2,Palpitation-3,Syncope-4,Fatigue-5,Limb weakness-6).In our study only shortness of breath, that is, without the other mentioned symptoms, was present in 11%. Only chest pain was present in 5%, only palpitation in 14%, only fatigue in 3%,and only limb weakness in 1%. Syncope in our study group was always present along with at least one another symptom. Only syncope, without another of the mentioned symptoms, was not observed in our study group.

All the other patients in our study had combinations of two or more symptoms in varying percentages.

Figure 3.Symptom profile



5.Etiological analysis:-

S.no	Etiology	Prevalence
1.	**Rheumatic heart disease**	77
2.	**Systemic hypertension**	7
3.	**Coronary heart disease**	4
4.	**Chronic obstructive pulmonary disease**	1
5.	**Hyperthyroidism**	2
6.	**HCM**	1
7.	**Atrial septal defect**	1
8.	**Mitral valve prolapse syndrome**	1
9.	**Dilated cardiomyopathy**	2
10.	**Drug induced**	1
11.	**Lone or Undetermined AF**	3

In our Study Rheumatic heart disease was the most common etiological factor associated with AF. It was observed in 77% of the patients . In our study the number of patients with Rheumatic heart disease were 77, and the remaining 23 cases had Non rheumatic etiological factors.

Females were predominant in the RHD group, out of the 77 patients with RHD, 63 were female,14 were male.

Among the Non RHD patients males were predominant. 18 were males,5 were females .

The second most common predisposing factor in our study was SHT. It was present in about 7%. About 4% of the cases of AF in our study had CAD as a possible etiological factor.

About 3% of the cases were due to “Lone or undetermined AF”. In this group, 1 patient had chronic use of alcohol, and presented with a history of binge alcohol intake associated with AF. That particular case can be considered as “Holiday heart syndrome”.

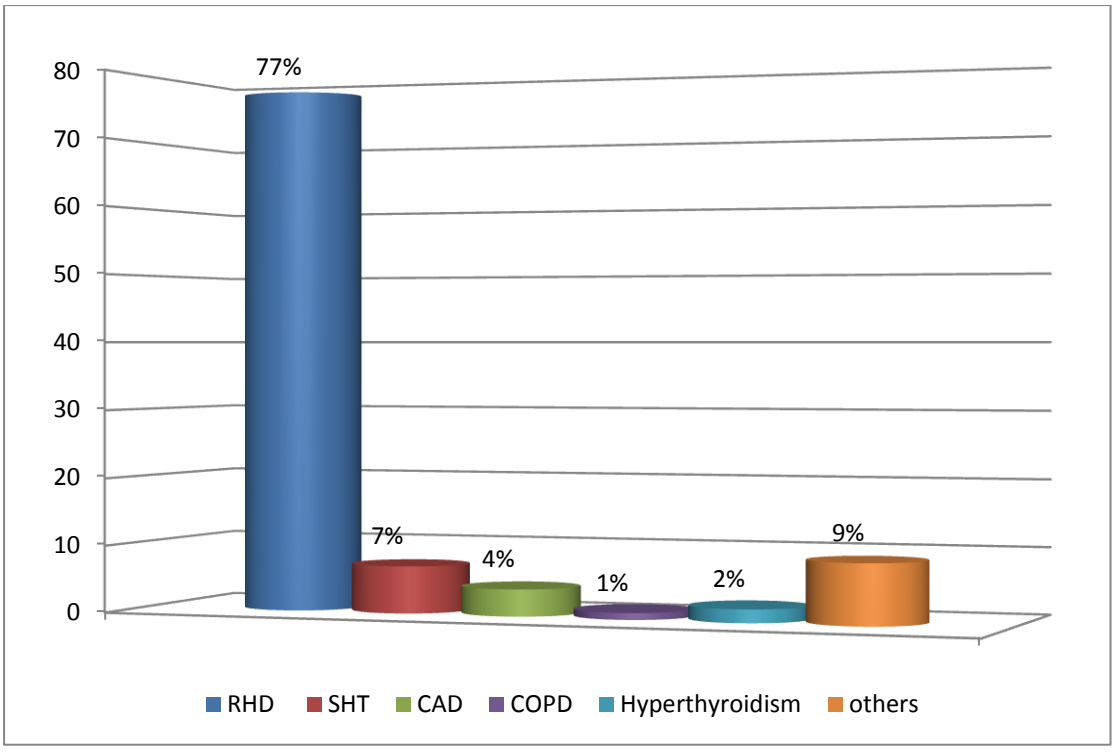
In the remaining 2 cases, because of the non-availability of required additional investigations (e.g.,’electrophysiological study’, ‘Holter monitoring’ etc..), we could not find the cause for AF.

About 2% of the cases were due to hyperthyroidism, Another 2% of the cases were due to Dilated cardiomyopathy.

All other etiological factors – Chronic obstructive pulmonary disease, Mitral valve prolapse syndrome, Atrial septal defect, Hypertrophic cardiomyopathy – were each present in 1% of the study population.

One patient had Bronchial asthma and had been given Theophylline injection before admission. This is probably a case of "Drug induced AF".

Figure 4.Etilogy of AF patients

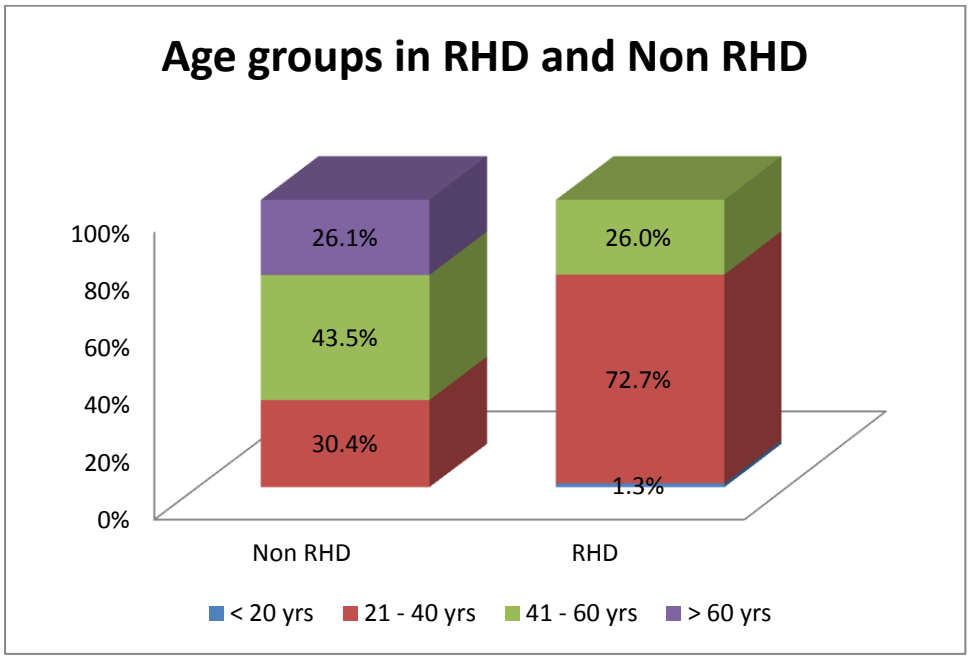


6.Age distribution Among RHD and Non RHD patients of AF:-

			RHD		Total
			N	Y	
AGE GROUP	< 20 yrs	Count	0	1	1
		%	0.0%	1.3%	1.0%
	21 - 40 yrs	Count	7	56	63
		%	30.4%	72.7%	63.0%
	41 - 60 yrs	Count	10	20	30
		%	43.5%	26.0%	30.0%
	> 60 yrs	Count	6	0	6
		%	26.1%	0.0%	6.0%
Total		Count	23	77	100
		%	100.0%	100.0%	100.0%

In the <20 years age group only one(1.3%) patient present,21-40years of age group(72.7%) there were present,41-60 years (26%),and in >60 years nil patient present. The relationship between age group versus RHD and Non RHD was found to be significant('P'value < .05)

Figure 5.Age groups in RHD and Non RHD

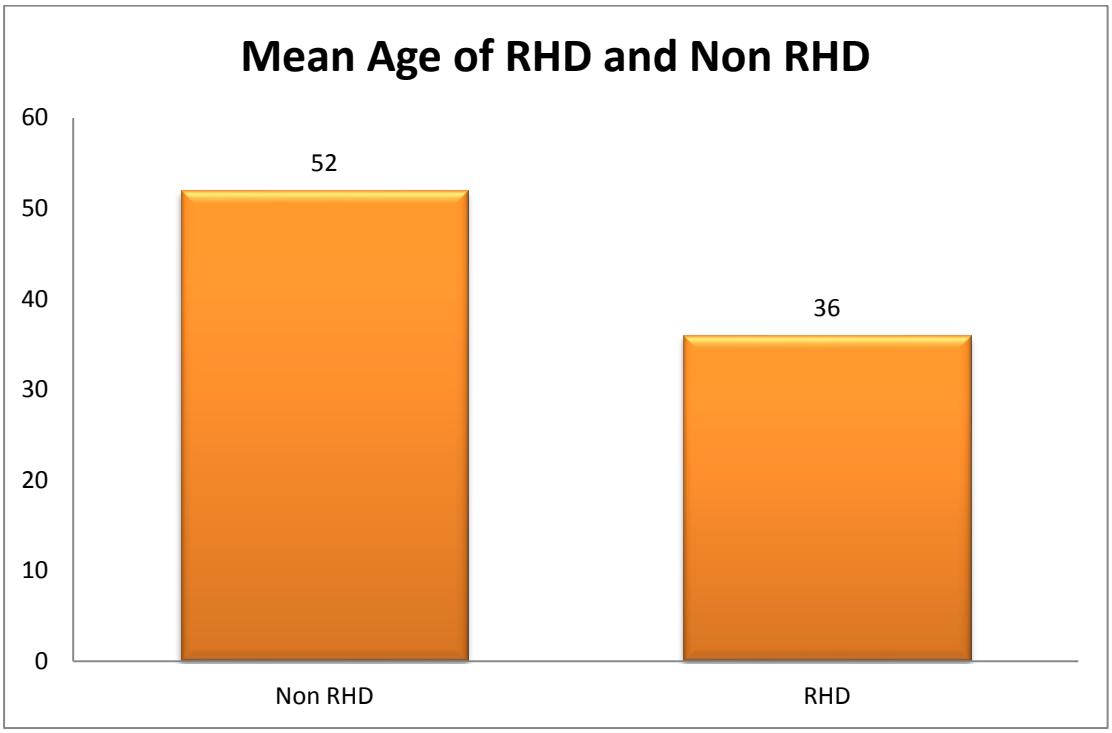


7.Mean Age of RHD and Non RHD Patients:

		N	Mean	Std. Deviation	Std. Error Mean
AGE	**Non RHD**	23	52	13.347	2.783
	RHD	77	36	7.970	.908

The mean age of RHD patient is 36,Non RHD patients 52.The relationship between Mean age versus RHD and Non RHD was found to be significant('P'value< .05)

Figure 6.Mean Age of RHD and Non RHD Patients



8.1Gender Distribution of patients of AF with RHD:-

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	F	63	81.8	81.8	81.8
	M	14	18.2	18.2	100.0
	Total	77	100.0	100.0	

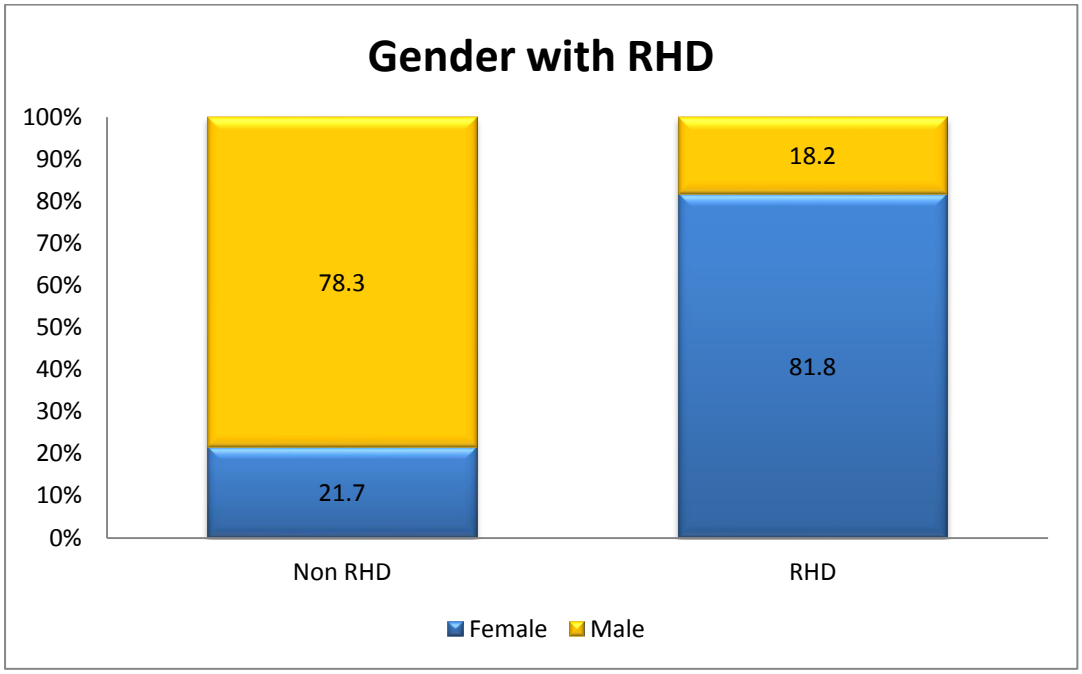
Females were predominant in the RHD group, out of the 77 patients with RHD, 63 were female,14 were male.

8.2Gender Distribution of patients of AF with Non RHD:-

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	F	5	21.7	21.7	21.7
	M	18	78.3	78.3	100.0
	Total	23	100.0	100.0	

Among the Non RHD patients males were predominant. 18 were males,5 were females.

Figure 7.Gender Distribution among RHD and Non RHD

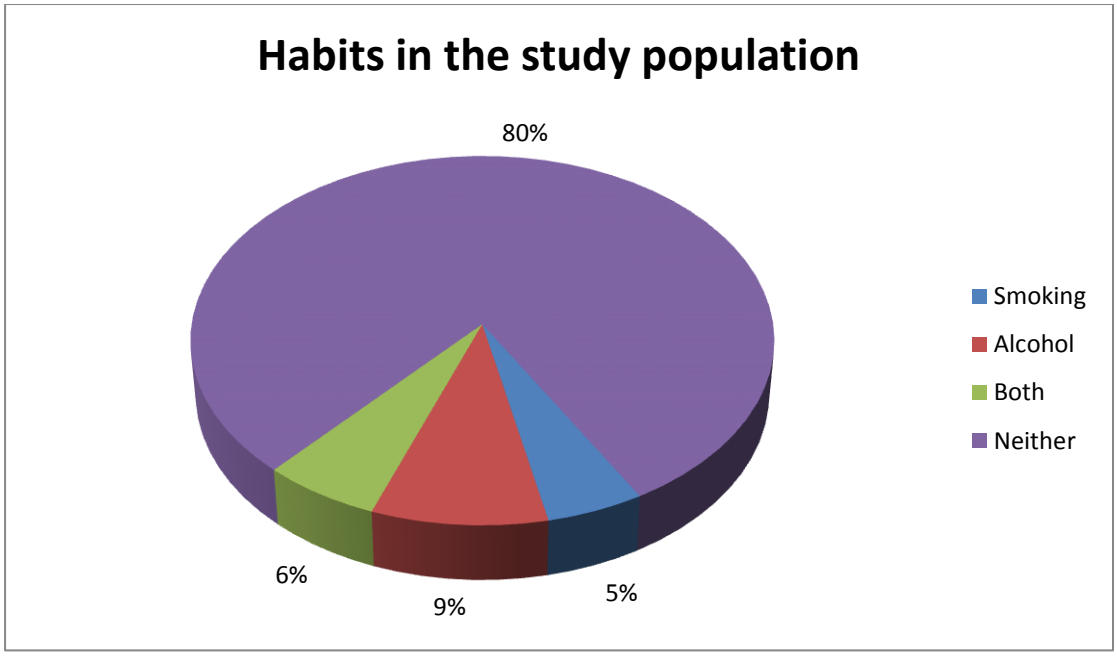


9.Substance Habit:-

S. no	Habits	Prevalence
1.	**Smoker**	5
2.	**Alcohol**	9
3.	**Alcohol and smoking**	6
4.	**No habits**	80

Among the study group 5 patients were smoker,9 patients were alcoholic,both habits present in 6 patients,nil habits present in 80 patients.

Figure 8.Habits in study population

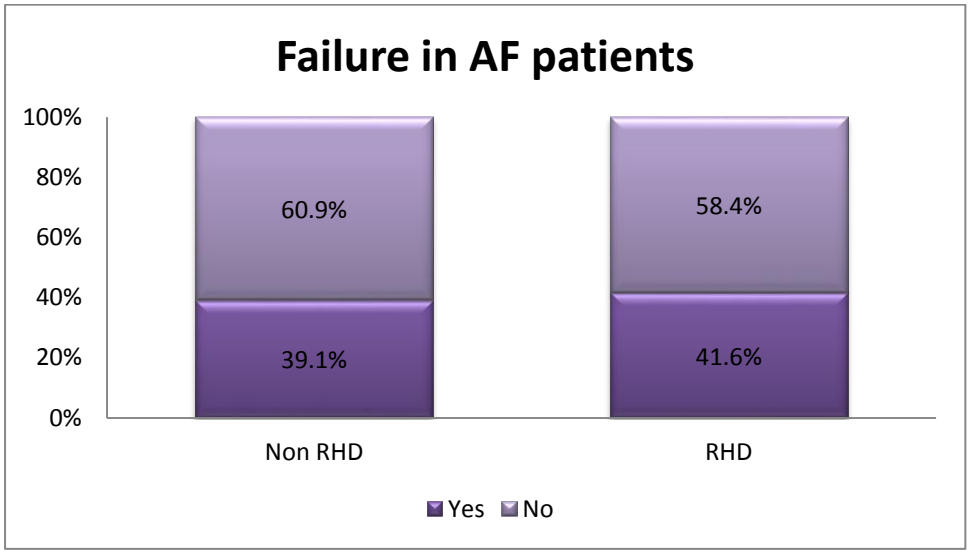


10.Failure analysis:-

			ETIOLOGY		Total
			Non RHD	RHD	
FAILURE	Yes	Count	9	32	41
		%	39.1%	41.6%	41.0%
	No	Count	14	45	59
		%	60.9%	58.4%	59.0%
Total		Count	23	77	100
		%	100.0%	100.0%	100.0%

Among the study group,41.6%(N=32) of patients with RHD presented with failure,39.1%(n=9) of patients with Non RHD presented with failure. The difference was statistically insignificant('P'value >.05).

Figure 9.Failure in AF patients



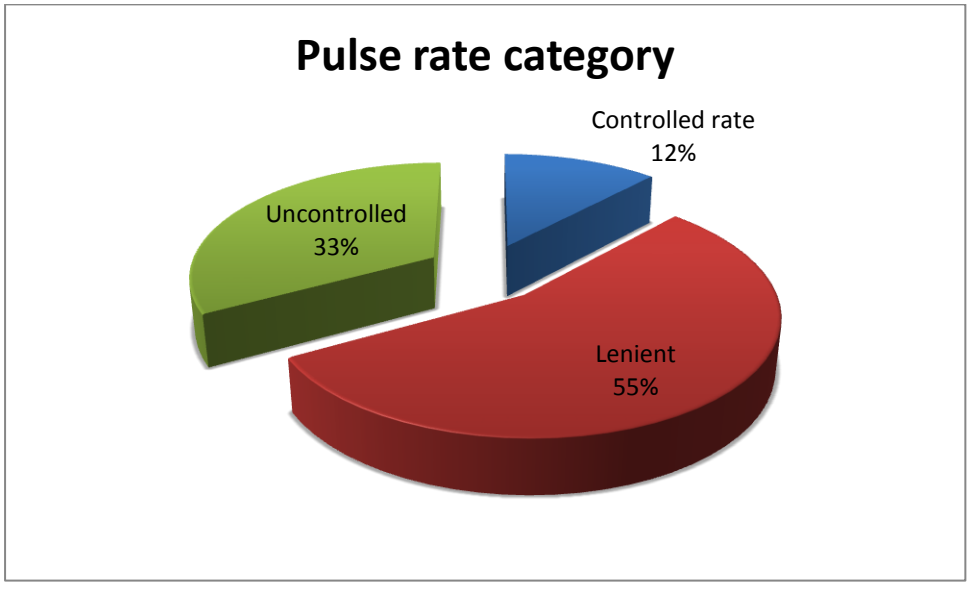
11.Pulse rate Analysis:-

11.1.In overall patients:-

Pulse rate category (Ventricular)	Frequency	Percent	Valid Percent	Cumulative Percent
Controlled	12	12.0	12.0	12.0
Lenient	55	55.0	55.0	67.0
Uncontrolled	33	33.0	33.0	100.0
Total	100	100.0	100.0	

In our study ,12% of the total patients presented with controlled ventricular rate (<80/bpm), 55% of the patients presented with lenient ventricular rate (<110/bpm) and the remaining 33% presented with uncontrolled ventricular rate (>110/bpm).

Figure 10.Pulse rate category



11.2. In RHD patients:-

Pulse rate category (ventricular)		Frequency	Percent	Valid Percent	Cumulative Percent
RHD	Controlled rate	11	14.3	14.3	14.3
	Lenient	43	55.8	55.8	70.1
	Uncontrolled	23	29.9	29.9	100.0
	Total	77	100.0	100.0	

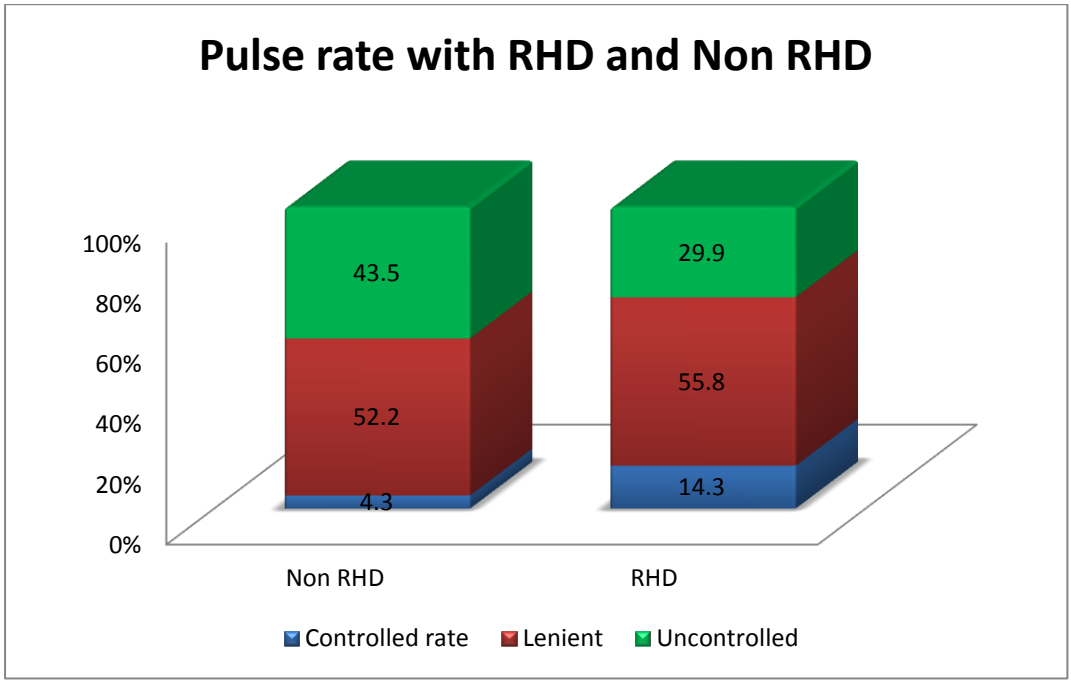
In RHD group patients, 14.3% (n=11) presented with controlled ventricular rate rate, 55.8% (n=43) presented with lenient ventricular rate rate, and 29.99%(n=23) with uncontrolled ventricular rate.

11.3. In Non RHD Patients:-

Pulse rate category (Ventricular)		Frequency	Percent	Valid Percent	Cumulative Percent
Non RHD	Controlled rate	1	4.3	4.3	4.3
	Lenient	12	52.2	52.2	56.5
	Uncontrolled	10	43.5	43.5	100.0
	Total	23	100.0	100.0	

In Non RHD group patients , 4.3% (n=1)of them presented with controlled ventricular rate, 52.2% (n=12) presented with lenient ventricular rate, remaining 43.5% (n=10) of them presented with uncontrolled ventricular rate.

Figure 11.Pulse rate with RHD and Non RHD



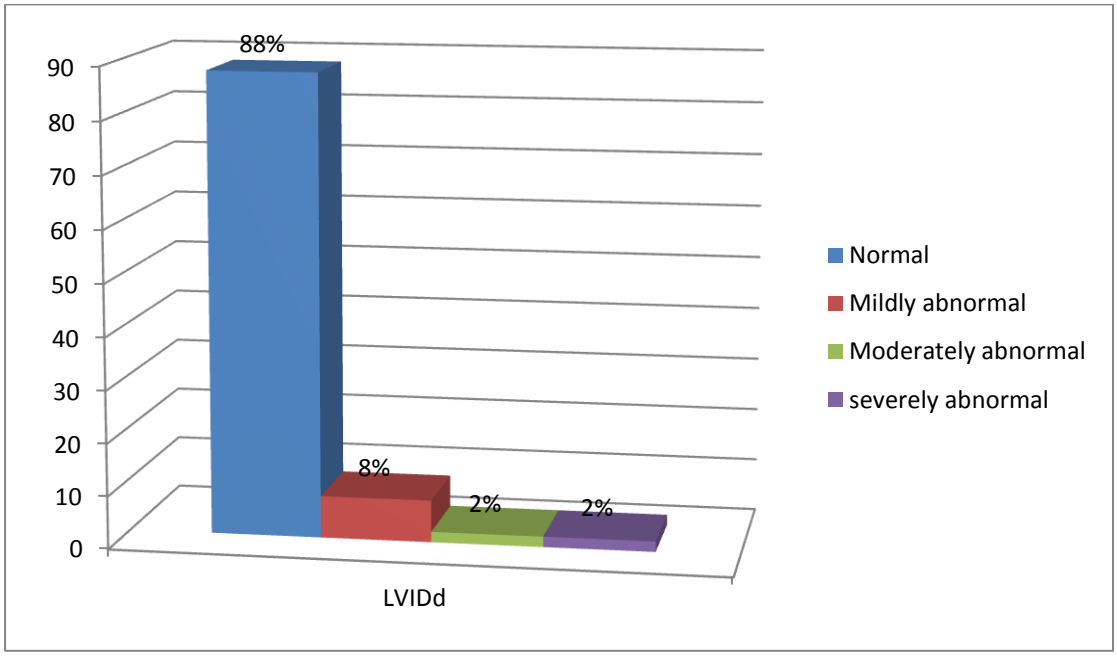
Transthoracic Echocardiography parameters analysis:-

1.Left Ventricular Internal Diamter(Cm) in diastole(LVIDd):-

S.no	Category	Prevalence
1.	**Normal**	88
2.	**Mildly abnormal**	8
3.	**Moderately abnormal**	2
4.	**Severely abnormal**	2

In our study population 88% of the people presented with normal LVIDd,8% of the patients with Mildly abnormal,2% of the patients with Moderately abnormal, and the remaining 2% of the patients presented with severely abnormal LVIDd.

Figure 1.Left ventricular internal diameter(Cm) in diastole

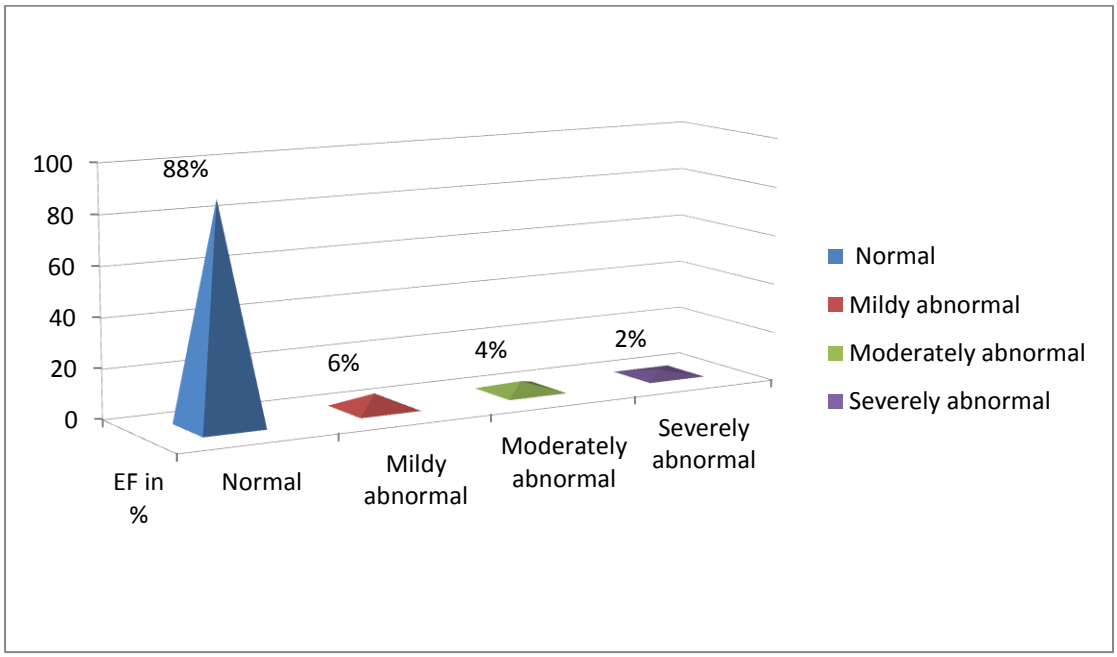


2.Ejection fraction in % (EF%-LV Systolic function):-

S.no	Category	Prevalence
1.	Normal	88
2.	Mildly abnormal	6
3.	Moderately abnormal	4
4.	Severely abnormal	2

In our study 88% of the people had normal EF,6% of the people had mildly abnormal,4% of the people had moderately abnormal, and the remaining 2% of them presented with severely abnormal EF

Figure 2.Ejection fraction in%(EF%-Left ventricular systolic function

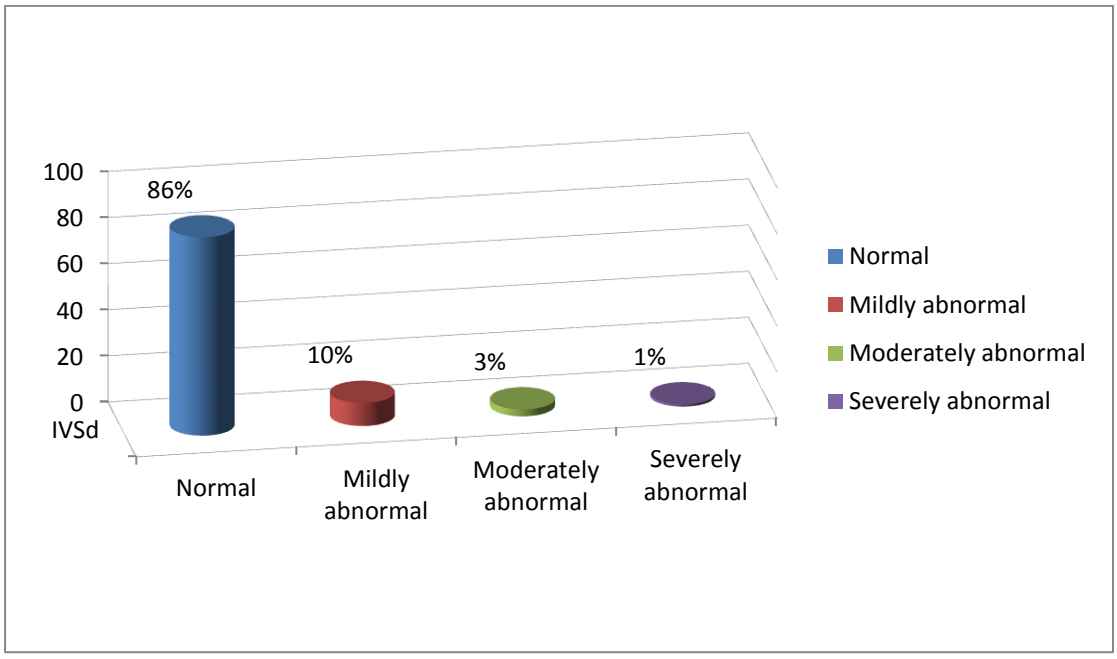


3.Interventricular septal thickness(Cm) in diastole (IVSd):-

S.no	Category	Prevalence
1.	**Normal**	86
2.	**Mildly abnormal**	10
3.	**Moderately abnormal**	3
4.	**Severely abnormal**	1

In our study 86% of them presented with normal IVSd,10% of the patients with mildly abnormal,3% of the patients with moderately abnormal, the remaining 1% of the patient presented with severely abnormal value.

Figure 3.Interventricular septal thickness(cm)in diastole

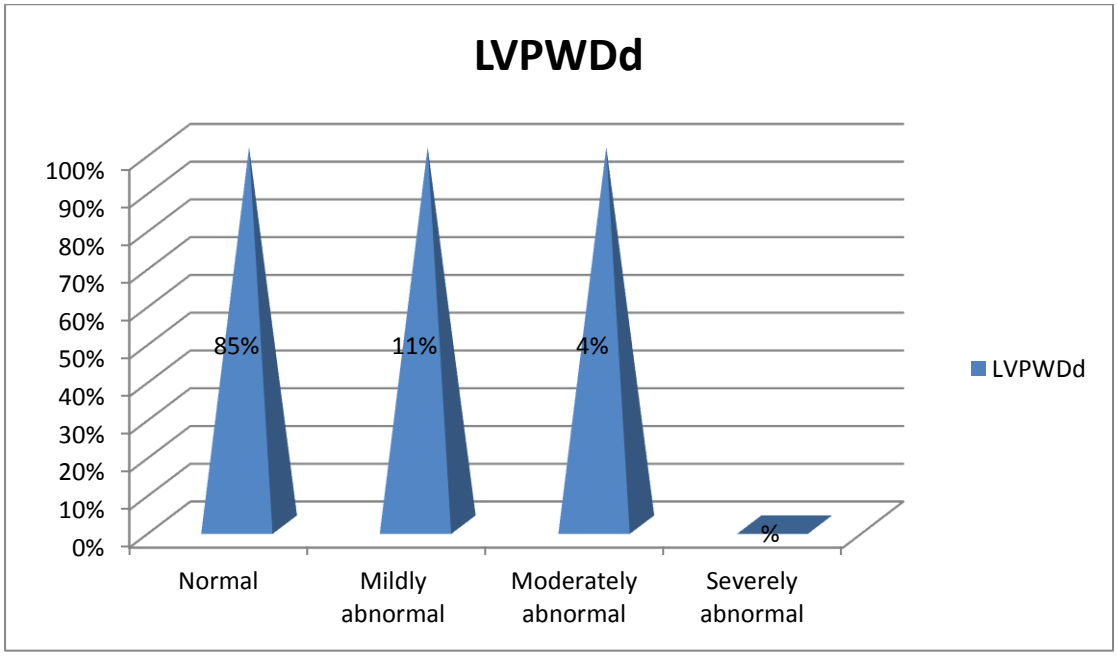


4.Left ventricular posterior thickness wall(Cm) in diastole(LVPWDd):-

S.no	Category	Prevalence
1.	**Normal**	85
2.	**Mildly abnormal**	11
3.	**Moderately abnormal**	4
4.	**Severely abnormal**	-

In our study 85% of them presented with normal LVPWDd,11% of the patients with mildly abnormal,4% of the patients with moderately abnormal, and no one had presented with severely abnormal value.

Figure 4.Left ventricular posterior wall thickness(cm) in diastole

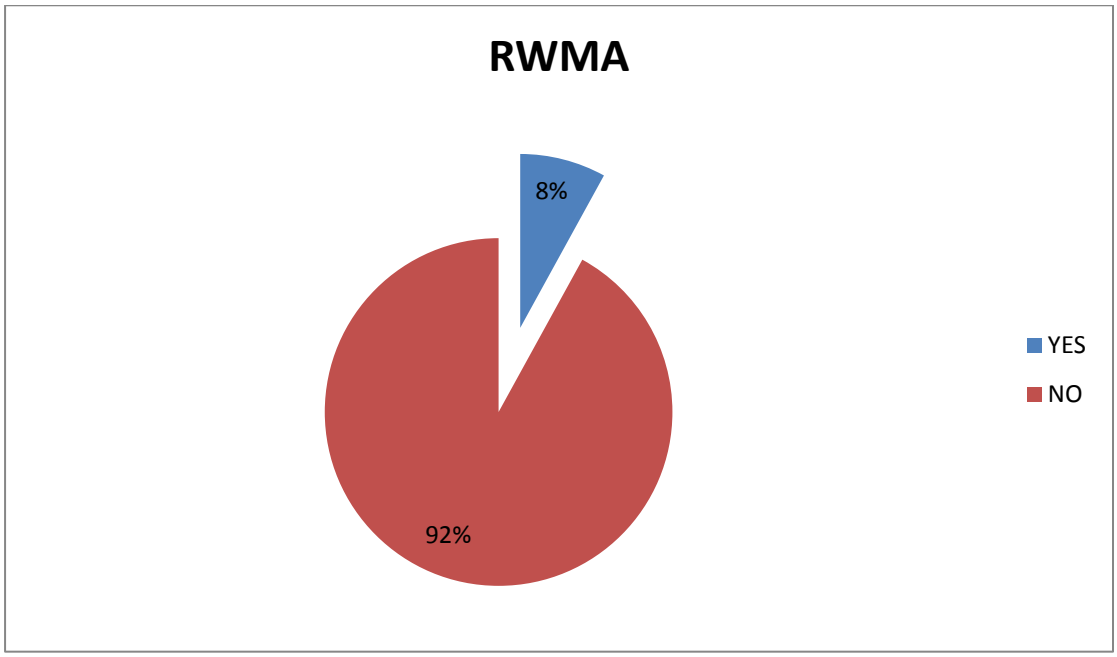


5.Regional wall motion abnormality (RWMA):-

S.no	RWMA	Prevalence
1	**YES**	8
2	**NO**	92

In our study 8% of people with presented with RWMA, and remaining 92% with no RWMA were present.

Figure 5.Regional wall motion abnormality

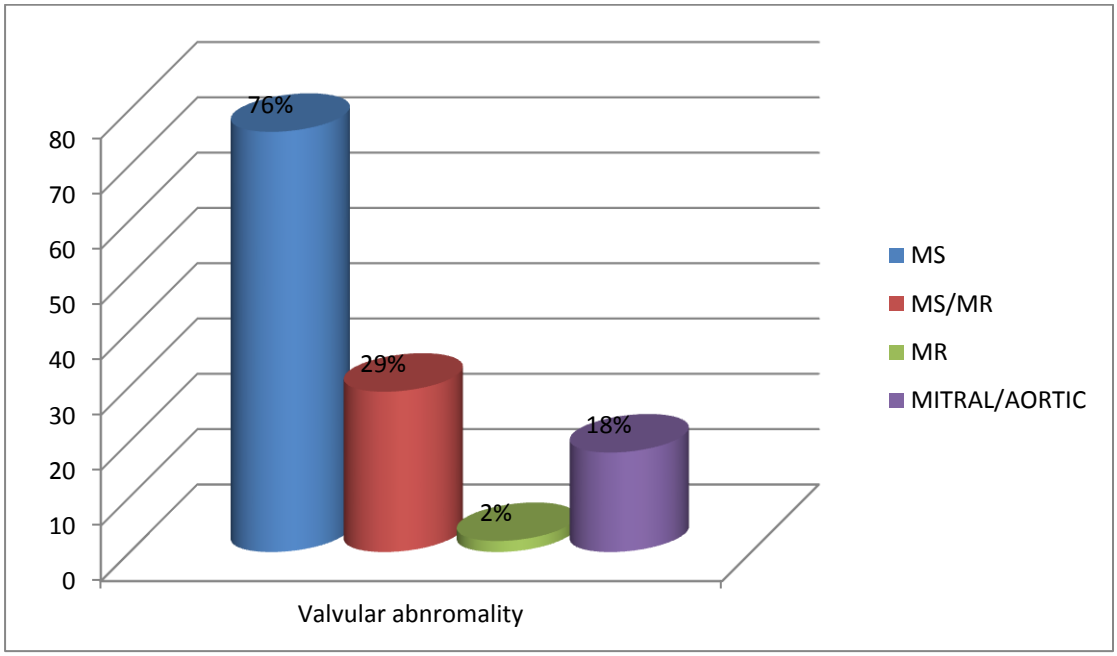


6.Valvular abnormality prevalence:-

S.No	Valvular abnromality	Prevalence
1.	**Isolated MS**	76
2.	**Both MS/MR**	29
3.	**Isolated MR**	2
4.	**Both Mitral/Aortic**	18

In our study isolated MS was present in 76% of the patients,29% of the people presented with both MS/MR, isolated MR was present in 2% of the aortic valve lesion.

Figure 6.Valvular abnormality prevalence

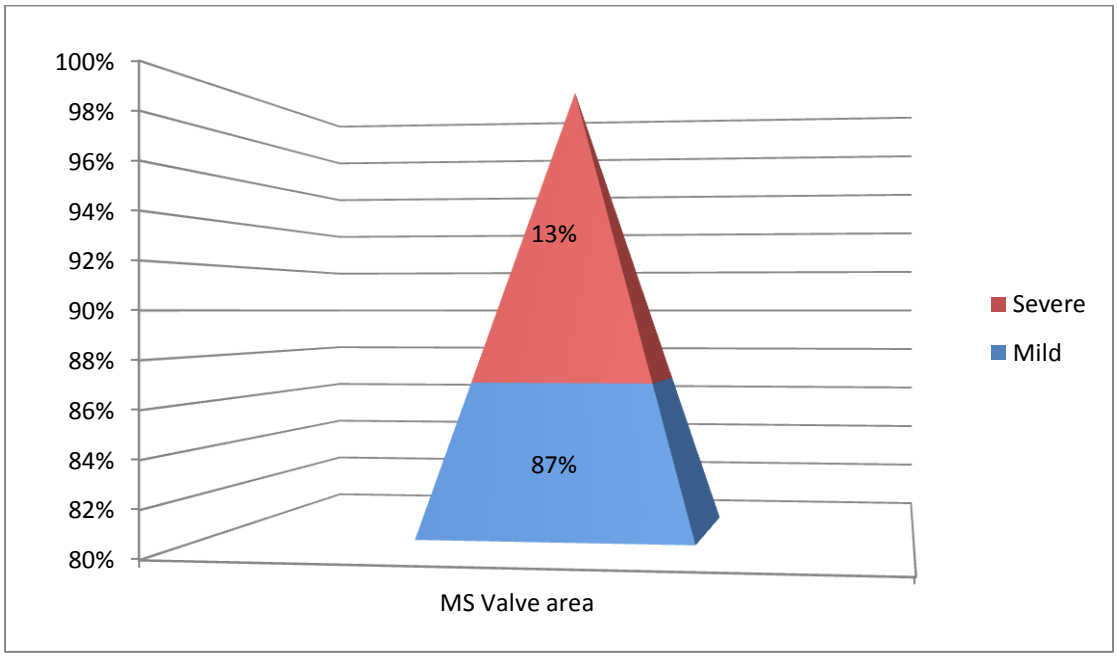


7.MS Severity according to valve area:-

S.no	MS Valve area in cm^2	Prevalence among those with MS
1	**Mild > 1.5**	86.8%(n=66)
2	**Severe < 1.5**	13.1%(n=10)

In our study population out of 76 patients, mild MS was present in 86.8% (n=66) of the patients, and the remaining 13.1% (n=10) cases presented with severe MS.

Figure 7.MS severity according to valve area

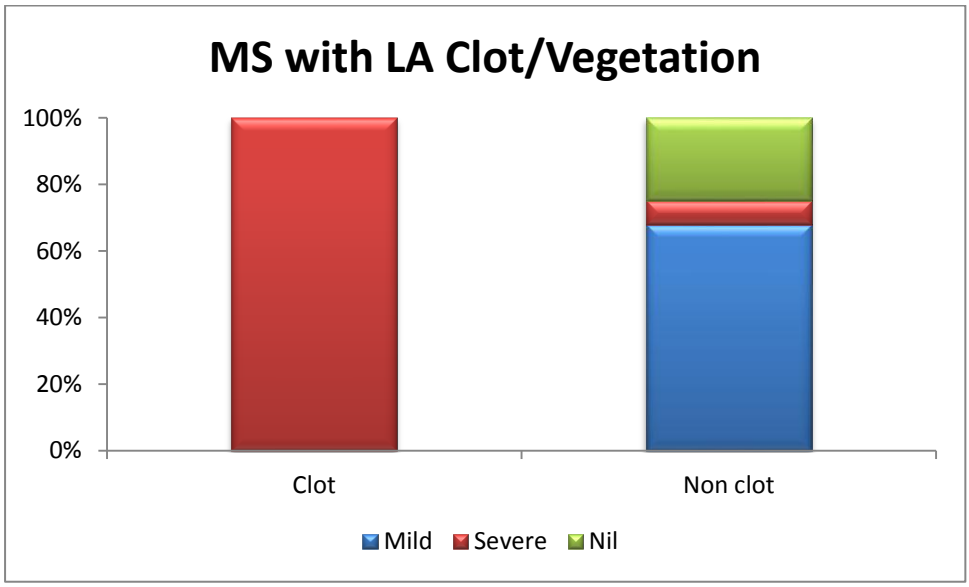


8.Severity of MS with LA clot/vegetation:-

			LA CLOT/VEGETATION		Total
			Yes	No	
MS	Mild	Count	0	66	66
		%	0.0%	68.0%	66.0%
	Severe	Count	3	7	10
		%	100.0%	7.2%	10.0%
	Nil	Count	0	24	24
		%	0.0%	24.7%	24.0%
Total		Count	3	97	100
		%	100.0%	100.0%	100.0%

There were 10 patients with severe MS in our study ,of whom 3 patients presented with LA clot. A statistically significant relationship was observed between MS and LA clot('P'value < .05)

Figure 8.Severity of MS with LA clot/Vegetation

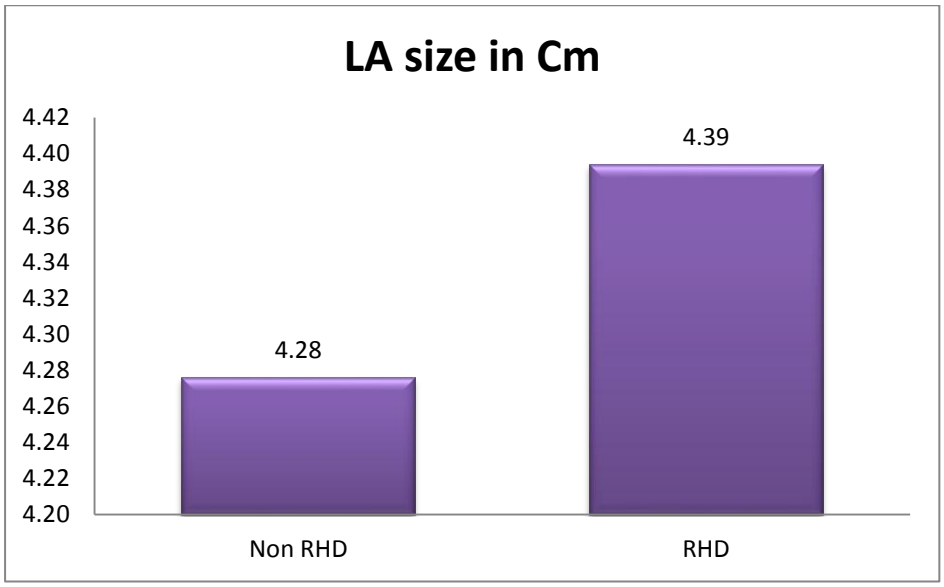


9.LA Size in cms:-

		Number of Patients	Mean	Std. Deviation	Std. Error Mean
LA SIZE cm	Non RHD	23	4.28	.45588	.09506
	RHD	77	4.39	.28372	.03233

In our study among RHD group of patients the Mean LA size was 4.39 cm,in Non RHD patients Mean LA size was 4.28 cm. No statistically significant difference was observed between the LA sizes of the RHD group and the Non-RHD group ('P'value > .05).

Figure 9.LA size (cm)



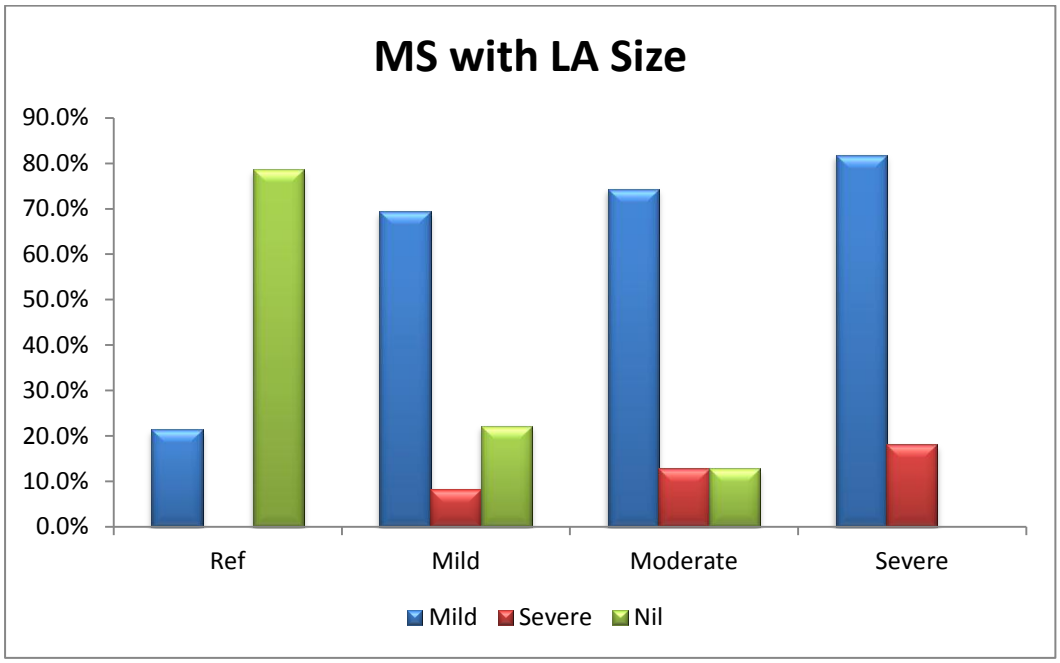
10.Comparison Between MS Valve severity and LA Size:-

MS with LA size			LA SIZE range				Total
			Ref	Mild	Moderate	Severe	
MS	Mild	Count	3	25	29	9	66
		%	21.4%	69.4%	74.4%	81.8%	66.0%
	Severe	Count	0	3	5	2	10
		%	0.0%	8.3%	12.8%	18.2%	10.0%
	Nil	Count	11	8	5	0	24
		%	78.6%	22.2%	12.8%	0.0%	24.0%
Total		Count	14	36	39	11	100
		%	100.0%	100.0%	100.0%	100.0%	100.0%

In our study, out of 66 patients with mild MS, LA size was in the normal range in 21.4% (n=3), was in the mildly abnormal range 69.4% (n=25) in 74.4% (n=29), and was in the severely abnormal range in 81.8% (n=9).

In our study, out of 10 patients with severe MS, no one had LA size in the normal. People who fell in the mildly abnormal range were 8.3% (n=3), moderately abnormal range were 12.8% (n=5), severely abnormal range were 18.2% (n=2). The relationship between the presence of MS and the LA size was found to be statistically significant (‘P’value <.05).

Figure 10.Comparison between MS severity and LA size



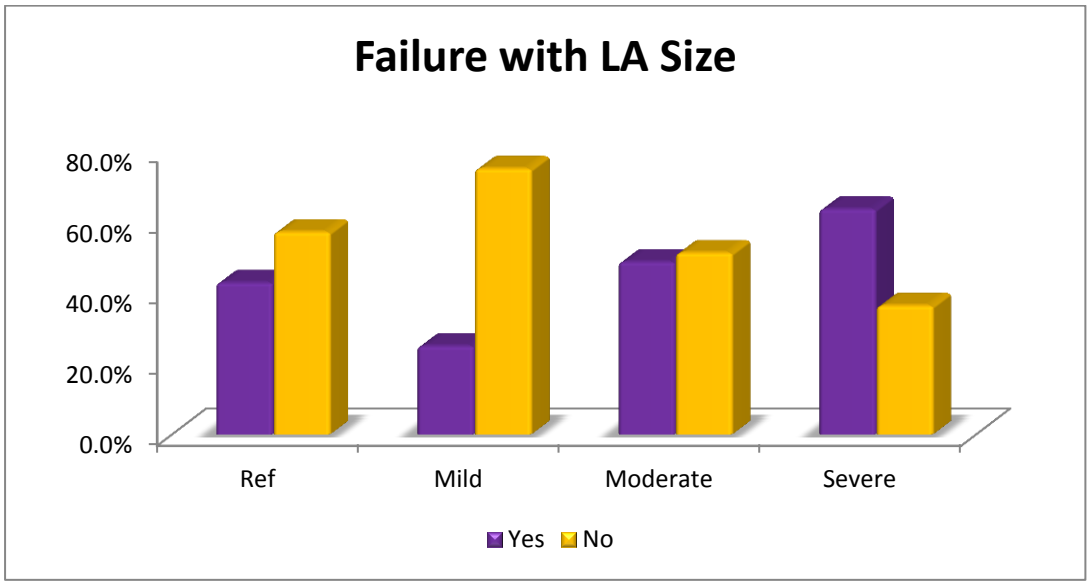
11.Comparison of Failure and LA size:-

			LA SIZE range				Total
			Ref	Mild	Moderate	Severe	
FAILURE	Yes	Count	6	9	19	7	41
		%	42.9%	25.0%	48.7%	63.6%	41.0%
	No	Count	8	27	20	4	59
		%	57.1%	75.0%	51.3%	36.4%	59.0%
Total		Count	**14**	**36**	**39**	**11**	**100**
		%	100.0%	100.0%	100.0%	100.0%	100.0%

In our study ,out of 41 patients with failure, LA size in the normal range in 42.9%(n=6) of the patients, in the mildly abnormal range 25.0%(n=9),in moderately abnormal range 48.7%(n=19),in the severely abnormal range 63.6%(n=7) of the patients there were present.

In our study ,out of 59 patients without failure, LA size in the normal range in 57.1%(n=8) of the patients, in the mildly abnormal range 75.0%(n=27),in moderately abnormal range 51.3%(n=20),in the severely abnormal range 36.4%(n=4) of the patients there were present. The relationship between failure and LA size was not found to be statistically significant (‘P’value >.05).

Figure11.Comparison of failure with LA size

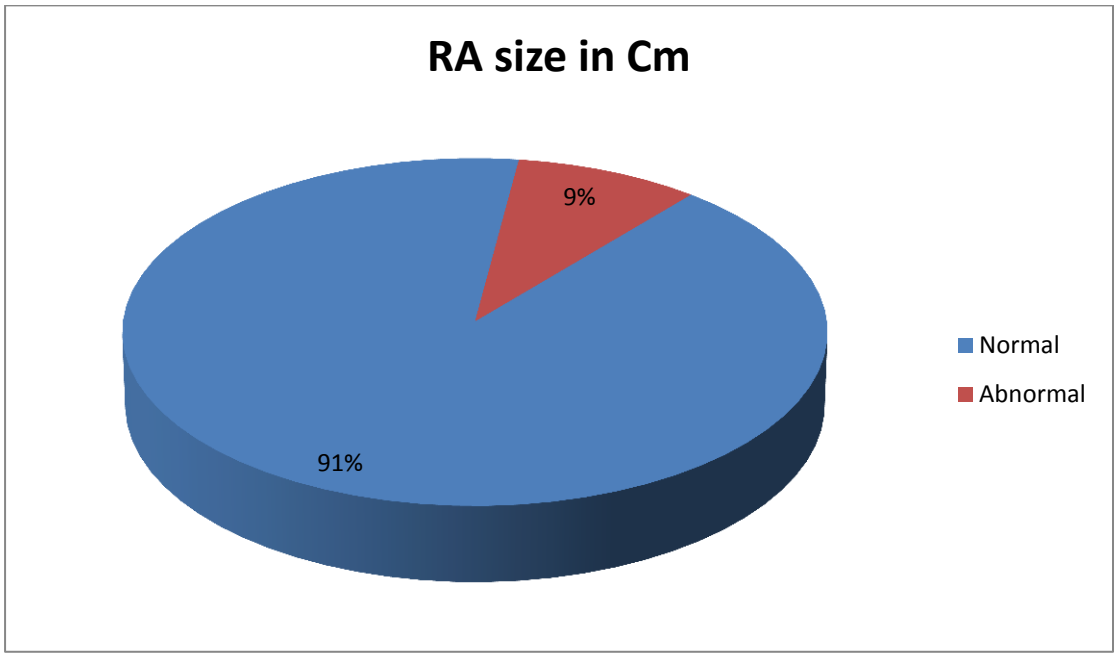


12.RA size:-

S.no	RA size Major Dimension in cm	Prevalence
1	**Normal < 5.3**	91
2	**Abnormal > 5.3**	9

In our study out of 100 patients RA size major dimension normal in 91% of the patients, in the remaining 9% of the patients RA size major dimension was abnormal.

Figure 12.RA size major dimension

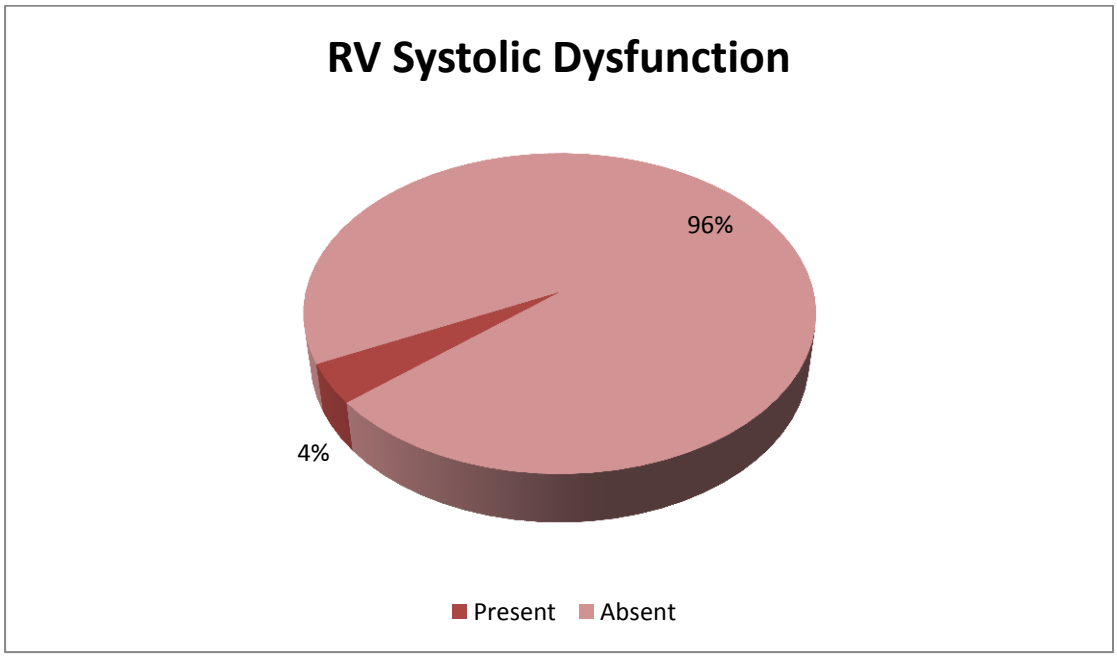


13.RV Systolic Dysfunction:

S.NO	RV Systolic Dysfunction	Prevalence
1	**Yes**	4
2	**No**	96

In our study RV systolic dysfunction was present in 4% of the patients, and the remaining 96% of the patients presented with normal RV systolic function.

Figure 13.RV systolic dysfunction

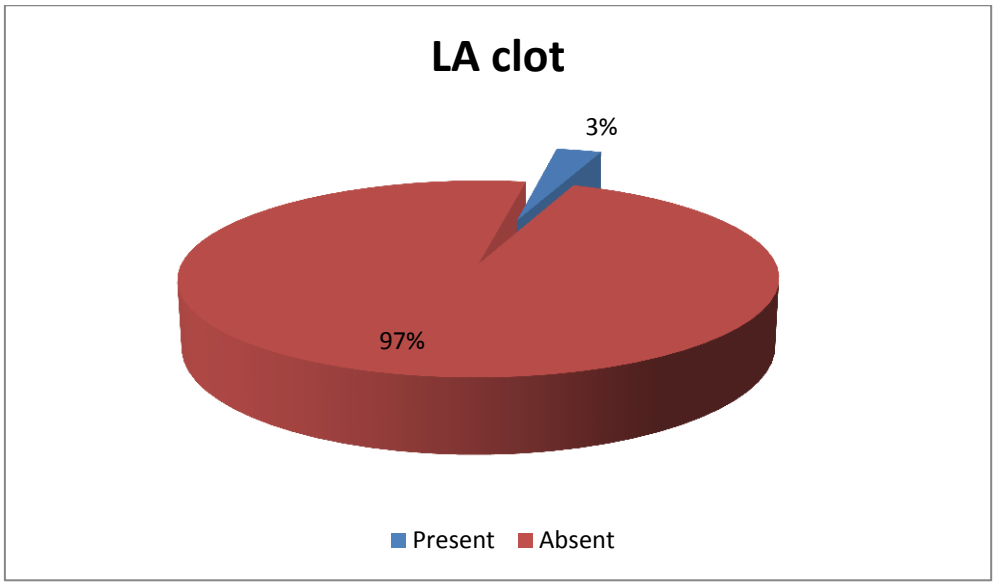


14.LA Clot:-

S.no	LA clot	Prevalence
1	**Present**	3
2	**Absent**	97

In our study out of 100 patients LA clot was present in 3% of the patients.

Figure 14. LA clot



DISCUSSION

In our study 100 patients with AF were included, the mean age of our study population for RHD 35.92,Non RHD 51.70.The relationship between Mean age versus RHD and Non RHD was found to be significant('P'value <.05)So in Non RHD patients AF occurs older age compared to RHD patients they were presented in younger age.

In our study females were more in number than males. Out of 100 total patients 68 were females 32 were males. In general male patients are more affected than female patients in AF but in our study female patients are more affected, since main etiology for AF in our study is RHD, this results conforms with the previous study by Dushyant S., et al[52].

In our study we divided the patients into 4 Age groups, as follows

1. < 20 years – 1
2. 21-40 years – 63
3. 41-60 years – 30
4. > 60 years – 6

In our study maximum number of patients were in the 21- 40 years age group, and less than 20 years only 1patient was present,> 60 years 6 patients were present .

Flaker, Greg C., et al study[70] shows 78% of the patients with 'SOB' and 11% of them were with chest pain, Tischler et al study[75] shows 'SOB' in 62% of patients,' palpitation' in 33% patients, and' syncope' in 12% patients, but in

our study predominant symptom was palpitation, which was present in about 72%,next comes shortness of breath which was present in about 66%,syncope accounted for 28%,and limb weakness was present in only about 1%.Many patients actually had multiple symptoms.

For the overall symptom analysis, we assigned a number for each symptom (SOB-1,Chest pain-2,Palpitation-3,Syncope-4,Fatigue-5,Limb weakness-6).In our study only shortness of breath, that is, without the other mentioned symptoms, was present in 11%. Only chest pain was present in 5%, only palpitation in 14%, only fatigue in 3%,and only limb weakness in 1%. Syncope in our study group was always present along with at least one another symptom. Only syncope, without another of the mentioned symptoms, was not observed in our study group.

All the other patients in our study had combinations of two or more symptoms in varying percentages.

In our Study Rheumatic heart disease was the most common etiological factor associated with AF. It was observed in 77% of the patients . In our study the number of patients with Rheumatic heart disease were 77, and the remaining 23 cases had Non rheumatic etiological factors. This results conforms with previous Kannel WB., et al and Diker E., et al studies[48,50].

Females were predominant[52] in the RHD group, out of the 77 patients with RHD, 63 were female,14 were male.

Among the Non RHD patients males were predominant. 18 were males,5 were females .

The second most common predisposing factor in our study was SHT. It was present in about 7%. This is in agreement with the study by Framingham[76], who also found a significant association between SHT and AF. About 4% of the cases of AF in our study had CAD as a possible etiological factor, and this conforms with the study by Kannel WB., et al and Crenshaw BS., et al[48,49].

About 3% of the cases were due to "Lone or undetermined AF". In this group, 1 patient had chronic use of alcohol65, and presented with a history of binge alcohol intake associated with AF. That particular case can be considered as "Holiday heart syndrome".

In the remaining 2 cases, because of the non-availability of required additional investigations (e.g., 'electrophysiological study', 'Holter monitoring 'etc..), we could not find the cause for AF.

About 2% of the cases were due to 'Hyperthyroidism', and this conforms with a previous study by Selmer C., et al[58]. Another 2% of the cases were due to 'Dilated cardiomyopathy' and this conforms with the study by Tsang TS.,et al[55].

All other etiological factors – 'Chronic obstructive pulmonary disease', 'Mitral valve prolapse syndrome', 'Atrial septal defect' – were each present in 1% of the study population. This conforms with the study by Khairy P., et al[56]

who studied patients with congenial heart diseases, and with the study by Robinson K., et al[53], who studied patients with 'Hypertrophic cardiomyopathy' contributing to AF.

One patient had 'Bronchial asthma' and had been given Theophylline injection before admission. This is probably a case of 'Drug induced AF'.

In the study group,41.6%(N=32) of patients with RHD presented with failure,39.1%(n=9) of patients with Non RHD presented with failure. The difference was statistically insignificant ('P'value >.05). This is in variation with the study done by Maisel WH.,et al[54],who found that failure was significantly more common in the RHD group.

In our study 88% of the people had normal EF,6% of the people had mildly abnormal,4% of the people had moderately abnormal, and the remaining 2% of them presented with severely abnormal EF, Presence of abnormal EF(LV systolic dysfunction) independently predicts the risk of stroke shown by Atrial fibrillation investigators study[69].

In our study isolated MS was present in 76% of the patients,29% of the people presented with both MS/MR, isolated MR was present in 2% of the people, and the remaining 18% of the people presented with both mitral and aortic valve lesion, this was conforms with previous Diker E et al study[50].

In our study population out of 76 patients, mild MS was present in 86.8% (n=66) of the patients, and the remaining 13.1%(n=10) cases presented with severe MS.A previous study by Habibzadeh F., et al also found that MS was most common subtype of valvular heart disease associated AF[51].

There were 10 patients with severe MS in our study , of whom 3 patients presented with LA clot. A statistically significant relationship was observed between MS and LA clot ('P'value < .05),this conforms with the study by Srimannarayana, J., et al[77]. Acar, J., et al study shows that the "sensitivity of TTE is 28% and specificity is 99%,and TEE has a sensitivity of 83%,and a specificity of 97% in detecting LA clot78.In our study, with TTE we observed LA clot in only 3patients.

In our study among RHD group of patients the Mean LA size was 4.39 cm, in Non RHD patients Mean LA size was 4.28 cm. No statistically significant difference was observed between the LA sizes of the RHD group and the Non-RHD group ('P'value > .05).This finding of ours disagrees with the finding by Flaker, Greg C., et al[70].

In our study, out of 66 patients with mild MS, LA size was in the normal range in 21.4% (n=3), was in the mildly abnormal range 69.4% (n=25) in 74.4% (n=29), and was in the severely abnormal range in 81.8% (n=9).

In our study, out of 10 patients with severe MS, no one had LA size in the normal. People who fell in the mildly abnormal range were 8.3% (n=3), moderately abnormal range were 12.8% (n=5), severely abnormal range were 18.2% (n=2). The relationship between the presence of MS and the LA size was found to be statistically significant ('P'value <.05). This conforms with the findings by Flaker, Greg C., et al[70], Henry WL.,et al[71],and Cabin HS.,et al[72].

SUMMARY

Atrial Fibrillation is the most commonly encountered quivering or irregular heart beat (arrhythmia) in our population.

The study was undertaken to study about clinical profile of AF and its transthoracic echocardiography presentation. Thus 100 patients with atrial fibrillation were taken up for study, After ethical committee clearance, and an informed consent, the patient's History, clinical and laboratory data were collected and analyzed statistically.

In our study females were more in number than males. Out of 100 total patients 68 were females,32 were males.

Rheumatic heart disease was the most common cause of AF in our study, systemic hypertension was the second most common cause for AF. In our study the number of patients with RHD were 77,and the remaining 23 cases had Non RHD etiological factors.

In our study isolated MS was present in 76 patients with RHD, and 1 patient with isolated MR, out of 76 patients, mild MS was present in 66 patients, and the remaining 10 cases presented with severe MS.

Thus rheumatic mitral stenosis was the most common cause of AF in our study with more female preponderance. Few Patients with severe MS presented with LA clot. We detected LA Clot only in a very few patients with AF because TTE has low sensitivity of detecting LA clot.

CONCLUSION

1. Patients with RHD etiology presented with AF in middle age, patients with Non RHD etiology presented in older age.

2. Female patients were more common then male patients.

3. Most common symptom in our study was palpitation.

4. Most common etiology was Rheumatic heart disease with Mitral stenosis.

5. Patient presented with AF of rheumatic origin were mostly female patients, whereas Non rheumatic origin were male patients.

6. Few Patients with severe MS presented with LA clot.

7. We detected LA Clot only in a very few patients with AF because TTE has low sensitivity of detecting LA clot.

LIMITATIONS OF THE STUDY

1. Hemodynamically unstable patients were excluded in our study so the relationship between LA clot and LV dysfunction and could not be completely assessed.

2. TTE was used in our study. TTE has low sensitivity of detecting LA clot, this was the reason for less number of patients with LA clot, in our study.

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ANNEXURES

ANNEXURE - I

INSTITUTIONAL ETHICS COMMITTEE
GOVT.KILPAUK MEDICAL COLLEGE,
CHENNAI-10
Protocol ID. No. 16/2016 Dt: 04.04.2016
CERTIFICATE OF APPROVAL

The Institutional Ethical Committee of Govt. Kilpauk Medical College, Chennai reviewed and discussed the application for approval " **A study of clinical profile of Atrial fibrillation and its transthoracic echocardiography presentation", a cross – scctional study at a tertiary care Hospital in Chennai** " - For Project Work submitted by **Dr.G.Ambedkar**, MD General Medicine, Govt. Kilpauk Medical College, Chennai – 10.

The Proposal is APPROVED.

The Institutional Ethical Committee expects to be informed about the progress of the study any Adverse Drug Reaction Occurring in the Course of the study any change in the protocol and patient information /informed consent and asks to be provided a copy of the final report.

DEAN.
Govt.Kilpauk Medical College,
Chennai – 10.

PC 2<ME I Section<Ethical Committee 1

ANNEXURE - II

PROFORMA

CLINICAL PROFILE OF ATRIAL FIBRILLATION AND ITS TRANSTHORACIC ECHOCARDIOGRAPHY PRESENTATION

Name:-

Age / Sex:-

I.P. No :-

Presenting complaints :-

Shortness of Breath :

Chest pain:

Palpitation:

Syncope :

Fatigue :

Weakness of limbs :

Past History:-

SHT:

RHD :

CAD:

COPD:

DM :

Others:-

Treatment History:-

General Examination:-

Consciousness: Pallor: Clubbing: Cyanosis: Pedal Edema: JVP:

Signs of Hyperthyroidism:

Vitals:-

Pulse Rate :

Pulse Deficit :

BP :

Respiratory Rate :

Examination of Systems:

CVS :

RS :

Abdomen :

CNS :

Investigations:-

CBC: RFT: Lipid Profile: Serum Electrolytes :

Free T3,T4,TSH (When Indicated) :

ECG : X-ray Chest:

Transthoracic Echocardiography:-

LVIDd : LVIDs: IVSd: LVPWd:

EF: RWMA: DOPPLER: MS: MR:
AORTIC VALVE:

TR: TRPG: PHT: PE:

LA Size: RA Size: RV Systolic function:

LA clot/Vegetation: LA Dilatation:

DIAGNOSIS:

ANNEXURE - III

சுயஒப்புதல் படிவம்

ஆய்வு செய்யப்படும் தலைப்பு:- "ஏட்ரியல் குறுநடுக்கத்தின் மருத்துவ சுயவிவரம் பற்றிய ஒரு ஆய்வு மற்றும் அதன் மார்பு வழி மின் ஒலி இதய வரைவி வழங்கல்".

இடம்: பொது மருத்துவ துறை,

அரசு கீழ்பாக்கம் மருத்துவக் கல்லூரி மருத்துவமனை,

சென்னை.

பங்குபெறுபவரின் பெயர் :

பங்குபெறுபவரின் வயது : **பங்குபெறுபவரின் எண் :**

மேலே குறிப்பிட்டுள்ள மருத்துவ ஆய்வின் விவரங்கள் எனக்கு விளக்கப்பட்டது. நான் இவ்வாய்வில் தன்னிச்சையாக பங்கேற்கிறேன். எந்த காரணத்தினாலோ எந்த சட்டசிக்கலுக்கும் உட்படாமல் நான் இவ்வாய்வில் இருந்து விலகிக்கொள்ளல்லாம் என்றும் அறிந்து கொண்டேன்.

இந்த ஆய்வு சம்பந்தமாகவோ, இதை சார்ந்து மேலும் ஆய்வு மேற்கொள்ளும்போதும் இந்த ஆய்வில்பங்கு பெறும் மருத்துவர் என்னுடைய மருத்துவ அறிக்கைகளை பார்ப்பதற்கு என் அனுமதி தேவையில்லை என அறிந்து கொள்கிறேன். இந்த ஆய்வின் மூலம் கிடைக்கும் தகவலையோ, முடிவையோ பயன்படுத்திக்கொள்ள மறுக்க மாட்டேன்.இந்த ஆய்வில் பங்கு கொள்ள ஒப்புக்கொள்கிறேன். இந்த ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேன் என்றும் உறுதியளிக்கிறேன்.

பங்கேற்பவரின் கையொப்பம் **ஆய்வாளரின் கையொப்பம்**

இடம் :

தேதி :

PATIENT CONSENT FORM

Study detail**"A Study Of Clinical Profile of Atrial Fibrillation and its Transthoracic Echocardiography Presentation'', a cross-sectional study at a Tertiary Care Hospital in Chennai"**

Study centre : GOVT.KILPAUK MEDICAL COLLEGE&HOSPITAL, CHENNAI

Patients Name :

Patients Age :

Identification Number :

I confirm that I have understood the purpose of procedure for the above study. I have the opportunity to ask question and all my questions and doubts have been answered to my complete satisfaction.

I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving reason, without my legal rights being affected.

I understand that sponsor of the clinical study, others working on the sponsor's behalf, the ethical committee and the regulatory authorities will not need my permission to look at my health records, both in respect of current study and any further research that may be conducted in relation to it, even if I withdraw from the study I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from this study.

I agree to take part in the above study and to comply with the instructions given during the study and faithfully cooperate with the study team and to immediately inform the study staff if I suffer from any deterioration in my health or well-being or any unexpected or unusual symptoms.

I hereby consent to participate in this study.

I hereby give permission to undergo complete clinical examination and diagnostic tests including hematological, biochemical, radiological tests.

Signature/thumb impression:

Patients Name and Address:

Signature of investigator :

Study investigator's Name : place: date:

ANNEXURE - IV

ஆராய்ச்சி தகவல் தாள்

சென்னை கீழ்பாக்கம் அரசு மருத்துவக் கல்லூரி மருத்துவமனையில் ஆராய்ச்சி ஒன்று நடைபெற்றுவருகிறது. **”ஏட்ரியல் குறுநடுக்கத்தின் மருத்துவ சுயவிவரம் பற்றிய ஒரு ஆய்வு மற்றும் அதன் மார்பு வழி மின் ஒலி இதய வரைவி வழங்கல்”** என்பதே இதன் தலைப்பாகும்.

நீங்களும் இந்த ஆராய்ச்சியில் பங்கேற்க நாங்கள் விரும்புகிறோம். முடிவுகளை அல்லது கருத்துக்களை வெளியிடும் போதோ அல்லது ஆராய்ச்சியின் போதோ தங்களது பெயரையோ அல்லது அடையாளங்களையோ வெளியிடமாட்டோம் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

இந்த ஆராய்ச்சியில் பங்கேற்பது தங்களுடைய விருப்பத்தின் பேரில் தான் இருக்கிறது. மேலும் நீங்கள் எந்நேரமும் இந்த ஆராய்ச்சியிலிருத்து பின்வாங்கலாம் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

இந்த சிறப்புப் பரிசோதனைகளின் முடிவுகளை ஆராய்ச்சியின் போது அல்லது ஆராய்ச்சியின் முடிவில் தங்களுக்கு அறிவிப்போம் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

ஆராய்ச்சியாளர் கையொப்பம்

பங்கேற்பாளர்கையொப்பம்

தேதி:

ANNEXURE - V

MASTER CHART

ANNEXURE - VI

KEY TO MASTER CHART

1. Sex:- Male – M , Female – F
2. Age group:- 1→ <20 yrs; 2 → 20-40 yrs ;3 → 40-60 yrs; 4 → >60 yrs
3. Symptoms:-

    1→ Shortness of breath

    2 → Chest pain

    3→ Palpitation

    4→ Syncope

    5→ Fatigue

    6 → Weakness of limbs

4. SHT → Systemic hypertension,

    RHD → Rheumatic Heart Disease

    CAD → Coronary heart disease , YES – Y, NO - N

    COPD → Chronic obstructive pulmonary disease

    DM → Diabetes mellitus
5. Hyperthyroidism : -YES – Y , NO – N
6. Others :-

    U – Undetermined OR Lone AF

    HCM – Hypertrophic cardiomyopathy

    MVPS - Mitral valve prolapse syndrome

    BA (DRU) - Bronchial asthma(Drug induced).

DCMP - Dilated cardiomyopathy

ASD – atrial septal defect

7. Habits :- Smoker – 1, Alcoholic – 2 ,nil – 3
8. Failure signs :- Yes – 1 , No – 2
9. PRcategory(Pulserate):- -

   1→<80bpm/min,2→<110bpm/min,3→>110bpm/min
10. LVIDd(Left ventricular internal Diameter in cm during diastole):-

	MEN	WOMEN
Reference range:	4.2-5.9 → 1	3.9-5.3→1
Mildly abnormal:	6.0-6.3 → 2	5.4-5.7→2
Moderately abnormal:	6.4-6.8→3	5.8-6.1→3
Severely abnormal:	≥ 6.9→4	≥ 6.2→4

11. EF (Ejection fraction %):-

    Both men and women have same values,

Reference range:	≥ 55→1
Mildly abnormal :	45-54→2
Moderately abnormal ;	30-44→3
Severely abnormal :	< 30→4

12. IVSd (Inter ventricular septal thickness in cm during Diastole):-

    LVPWd(Left ventricular posterior Wall thickness in cm during Diastole)

    Both are having same values

	MEN	WOMEN
Reference range:	0.6-1.0 → 1	0.6- 0.9 →1
Mildly abnormal:	1.1-1.3 → 2	1.0-1.2→2
Moderately abnormal :	1.4-1.6 →3	1.3-1.5 →3
Severely abnormal :	≥ 1.7→ 4	≥1.6 →4

13. RWMW(Regional Wall Motion Abnormality):- — YES → 1, NO → 2
14. MS(Mitral stenosis):-

    Mild - >1.5 cm^2 → 1

Severe - $< 1.5\ cm^2 \rightarrow 2$

15. MS/MR(Mitral stenosis /Mitral regurgitation): -Present →1, Absent →2
16. MR (Mitral regurgitation):- Present → 1, Absent → 2
17. MITRAL/AORTIC(Both Mitral and Aortic Valve involvement):-

    Present → 1, Absent → 2
18. LA SIZE(Left Atrium Diameter in cm)

	MEN	WOMEN
Reference range:	3.0-4.0→ 1	2.7-3.8→1
Mildly abnormal:	4.1-4.6→ 2	3.9-4.2→2
Moderately abnormal:	4.7-5.2→3	4.3-4.6→3
Severely abnormal :	≥ 5.3→ 4	≥4.7 →4

19. RA SIZE(Right Atrium Major Dimension in cm):-

    Normal < 5.3 → 1

    Abnomal > 5.3 → 2

20. RV(Right ventricular) Systolic Dysfuntion:-

    1→YES

    2→NO
21. LA (Left atrium)Clot :-

    1→YES

    2→NO

S.NO	AGE	AGE GROUP	SEX	SYMPTOMS	SHT	RHD	CAD	COPD	DM	HYPERTHYROID	OTHERS	HABITS	FAILURE	PR CATEGORY	LVIDd	EF %	IVSd	LVPWDd	RWMA	MS	MS/MR	MR	MITRAL/ AORTIC	LA SIZE	RA SIZE	RV SYSTOLIC DYSFUNCTION	LA CLOT /VEGETATION
1	42	3	M	1+3	N	Y	N	N	N	N	—	2	1	1	1	1	1	1	2	1	2	2	1	2	1	2	2
2	60	3	M	2	N	N	Y	N	N	N	—	2	2	2	1	1	2	1	2	3	2	2	2	2	1	2	2
3	50	3	F	2	Y	N	N	N	N	N	—	1	2	2	1	1	2	2	2	3	2	2	2	2	1	2	2
4	68	4	M	2	Y	N	N	N	N	N	—	1+2	2	1	1	1	3	3	2	3	2	2	2	2	1	2	2
5	60	3	F	1+2+3	Y	N	N	N	N	N	—	3	1	1	2	2	2	2	2	3	2	2	2	1	1	2	2
6	49	3	M	1+3	N	N	N	N	N	N	U	1	2	1	1	1	1	1	2	3	2	2	2	1	1	2	2
7	36	2	F	1+3	N	Y	N	N	N	N	—	3	1	1	1	1	1	1	2	1	1	2	2	3	1	2	2
8	25	2	M	1	N	Y	N	N	N	N	—	3	1	2	1	1	1	1	2	1	2	2	1	2	1	2	2
9	36	2	M	1+2+3+5	N	Y	N	N	N	N	—	3	1	1	1	1	2	1	2	1	1	2	2	2	1	2	2
10	39	2	F	1+2+5	N	Y	N	N	Y	N	—	3	1	2	1	1	2	2	2	2	2	2	2	3	1	2	1
11	19	1	F	3	N	Y	N	N	N	N	—	3	2	1	1	1	1	1	2	1	1	2	2	2	1	2	2
12	29	2	M	1	N	Y	N	N	N	N	—	2	2	2	1	1	1	1	2	3	2	2	2	2	1	2	2
13	58	3	M	1+2	Y	N	Y	N	N	N	—	1+2	1	2	2	3	3	3	1	3	2	2	2	3	1	2	2
14	33	2	M	1+3	N	Y	N	N	N	N	—	3	1	1	1	1	1	1	2	1	2	2	1	3	1	2	2
15	27	2	F	1	N	Y	N	N	N	N	—	3	1	2	1	1	1	1	2	1	2	2	2	3	1	2	2
16	40	2	M	1+3	N	N	N	N	Y	N	HCM	1+2	2	1	2	1	4	2	2	3	2	2	2	2	1	2	2
17	32	2	F	3+5	N	Y	N	N	N	N	—	3	2	1	1	1	1	1	2	1	2	2	2	1	1	2	2
18	39	2	F	1	N	Y	N	N	Y	N	—	3	1	2	1	1	1	1	2	1	2	2	1	2	1	2	2
19	20	2	F	1+2	N	Y	N	N	N	N	—	3	1	2	1	1	1	1	2	1	1	2	2	3	1	2	2
20	21	2	F	1+3+5	N	Y	N	N	N	N	—	3	1	2	1	1	1	1	2	1	1	2	2	3	1	2	2
21	26	2	F	1+3	N	Y	N	N	N	N	—	3	2	1	1	1	1	1	2	1	2	2	2	2	1	2	2
22	29	2	M	2+3	N	N	N	N	N	N	MVPS	3	2	2	2	1	1	1	2	3	2	1	2	2	1	2	2
23	34	2	F	1+2	N	Y	N	N	N	N	—	3	1	1	1	1	1	1	2	1	2	2	2	2	1	2	2
24	38	2	M	3	N	N	N	N	N	N	U	3	2	2	1	1	1	1	2	3	2	2	2	1	1	2	2
25	45	3	M	3	N	N	N	N	N	N	—	2	2	1	1	1	1	1	2	3	2	2	2	1	1	2	2
26	41	3	F	1+5	N	Y	N	N	N	N	—	3	2	2	1	1	1	1	2	1	1	2	2	3	1	2	2
27	25	2	F	1+3	N	Y	N	N	N	N	—	3	2	2	1	1	1	1	2	2	1	2	2	3	2	2	2
28	23	2	F	3	N	Y	N	N	N	N	—	3	2	1	1	1	1	1	2	1	1	2	2	2	1	2	2
29	40	2	F	1+3	N	N	N	N	N	N	BA(DRU)	3	2	2	1	1	1	1	2	3	2	2	2	1	1	2	2
30	35	2	F	1+4+5	N	Y	N	N	N	N	—	3	1	2	1	1	1	1	2	2	1	2	2	2	2	1	2
31	39	2	F	3	N	Y	N	N	N	N	—	3	2	1	1	1	1	1	2	1	1	2	2	2	1	2	2
32	43	3	M	1+2+3+5	N	Y	N	N	Y	N	—	2	1	1	1	1	1	1	2	2	2	2	1	2	2	2	2
33	29	2	F	1+5	N	Y	N	N	N	N	—	3	2	2	1	1	1	1	2	1	2	2	2	2	1	2	2
34	35	2	F	1+2+3	N	Y	N	N	N	N	—	3	1	1	1	1	1	1	2	1	2	2	2	2	1	2	2
35	38	2	F	1+2+4+5	N	Y	N	N	Y	N	—	3	2	2	1	1	1	1	2	1	2	2	1	3	1	2	2
36	29	2	F	3	N	Y	N	N	N	N	—	3	2	1	1	1	1	1	2	1	2	2	2	3	1	2	2
37	65	4	M	1+2+3+5	N	N	N	N	N	N	DCMP	1+2	1	1	3	4	1	1	1	3	2	2	2	3	1	2	2
38	27	2	F	3+5	N	Y	N	N	N	N	—	3	2	1	1	1	1	1	2	1	2	2	2	3	1	2	2
39	32	2	F	1+2+3+5	N	Y	N	N	N	N	—	3	1	2	1	1	1	1	2	1	2	2	1	1	1	2	2
40	37	2	M	7	N	Y	N	N	N	N	—	3	2	2	1	1	1	1	2	1	2	2	2	1	1	2	2
41	28	2	F	2+3	N	Y	N	N	N	N	—	3	2	2	1	1	1	1	2	1	1	2	2	2	1	2	2
42	40	2	M	1+2	Y	Y	Y	N	Y	N	—	2	1	1	1	3	2	2	1	1	2	2	1	4	1	2	2
43	42	3	F	1	N	Y	N	N	Y	N	—	3	2	2	1	1	1	1	2	1	2	2	2	3	1	2	2
44	53	3	F	1	N	Y	N	N	Y	N	—	3	2	2	1	1	1	1	2	1	1	2	2	3	1	2	2
45	27	2	F	3	N	Y	N	N	N	N	—	3	2	2	1	1	1	1	2	1	1	2	2	3	1	2	2
46	46	3	M	1+3	Y	N	N	N	N	N	—	2	2	2	1	1	3	3	2	3	2	2	2	2	1	2	2
47	40	2	F	1	N	Y	N	N	Y	N	—	3	2	2	1	1	1	1	2	1	1	2	2	3	1	2	2
48	47	3	F	1+2+5	N	Y	N	N	N	N	—	3	1	2	1	1	1	1	2	1	2	2	1	3	1	2	2
49	42	3	F	1+2+3+5	N	Y	N	N	Y	N	—	3	2	2	1	1	1	1	2	2	1	2	2	3	2	1	1
50	70	4	M	1+3	N	N	N	Y	N	N	—	1	1	1	1	2	1	2	2	3	2	2	2	1	2	2	2
51	40	2	F	1+2+3+4+5	N	Y	N	N	Y	N	—	3	1	2	1	1	1	1	2	1	1	2	1	4	1	2	2
52	37	2	F	1+5	N	Y	N	N	N	N	—	3	2	1	1	1	1	1	2	2	2	2	2	3	2	2	2
53	46	3	F	2+3	N	Y	N	N	Y	N	—	3	2	2	1	1	1	1	2	1	1	2	2	2	1	2	2
54	30	2	F	1	N	Y	N	N	N	N	—	3	2	2	1	1	1	1	2	1	2	1	2	2	1	2	2

S.NO	AGE	AGE GROUP	SEX	SYMPTOMS	SHT	RHD	CAD	COPD	DM	HYPERTHYROID	OTHERS	HABITS	FAILURE	PR CATEGORY	LVIDd	EF %	IVSd	LVPWDd	RWMA	MS	MS/MR	MR	MITRAL/ AORTIC	LA SIZE	RA SIZE	RV SYSTOLIC DYSFUNCTION	LA CLOT /VEGETATION
55	40	2	M	1+2+3	N	Y	N	N	N	N	—	2	1	3	2	1	1	1	2	1	1	2	2	3	1	2	2
56	23	2	M	7	N	Y	N	N	N	N	—	3	2	1	1	1	1	1	2	1	2	2	2	2	1	2	2
57	36	2	F	1+3	N	Y	N	N	N	N	—	3	1	3	1	1	2	2	2	1	1	2	2	3	1	2	2
58	45	3	M	1+2	N	N	Y	N	Y	N	—	3	1	2	1	2	1	1	1	3	2	2	2	1	1	2	2
59	31	2	F	2+3	N	Y	N	N	N	N	—	3	2	2	1	1	1	1	2	1	2	2	2	2	1	2	2
60	28	2	F	5	N	Y	N	N	N	N	—	3	2	2	1	1	1	1	2	1	2	2	2	2	1	2	2
61	40	2	F	1+2+4	N	Y	N	N	N	N	—	3	1	3	1	1	1	1	2	2	1	2	1	4	2	1	2
62	39	2	M	3	N	N	N	N	N	N	U	1	2	3	1	1	1	1	2	3	2	2	2	1	1	2	2
63	35	2	F	1+3	N	Y	N	N	N	N	—	3	2	2	1	1	1	1	2	1	2	2	2	2	1	2	2
64	37	2	F	3+5	N	Y	N	N	N	N	—	3	2	2	1	1	1	1	2	1	2	2	2	2	1	2	2
65	63	4	M	1+3+5	N	N	N	N	Y	N	DCMP	1+2	1	2	4	3	2	2	1	3	2	2	2	3	1	2	2
66	40	2	F	1+2+3+5	N	Y	N	N	Y	N	—	3	1	2	1	1	1	1	2	1	1	2	1	3	1	2	2
67	29	2	F	1+3	N	Y	N	N	N	N	—	3	1	3	1	1	1	1	2	1	2	2	2	3	1	2	2
68	41	3	F	1+2	N	Y	N	N	N	N	—	3	2	1	1	1	1	1	2	1	2	2	2	3	1	2	2
69	37	2	F	1+2+3	N	Y	N	N	N	N	—	3	1	2	1	1	1	1	2	1	1	2	2	4	1	2	2
70	37	2	F	3+5	N	Y	N	N	Y	N	—	3	2	3	1	1	1	1	2	1	2	2	2	3	1	2	2
71	39	2	F	3	N	N	N	N	N	Y	—	3	2	3	1	1	1	1	2	3	2	2	2	1	1	2	2
72	40	2	M	1+3	N	Y	N	N	N	N	—	3	2	2	1	1	1	1	2	1	2	2	2	2	1	2	2
73	33	2	F	1	N	Y	N	N	N	N	—	3	2	2	1	1	1	1	2	1	2	2	2	2	1	2	2
74	52	3	F	1+2+5	N	Y	N	N	Y	N	—	3	1	2	3	3	2	3	1	1	2	2	1	3	1	2	2
75	76	4	M	3	N	N	N	Y	N	N	—	1	1	3	2	2	1	1	2	3	2	2	2	1	2	1	2
76	30	2	F	3	N	Y	N	N	N	N	—	3	2	2	1	1	1	1	2	1	2	2	2	4	1	2	2
77	31	2	F	1+3	N	Y	N	N	N	N	—	3	2	2	1	1	1	1	2	1	2	2	2	2	1	2	2
78	29	2	F	1+3	N	Y	N	N	N	N	—	3	2	2	1	2	1	1	2	1	1	2	2	4	1	2	2
79	39	2	M	3	N	Y	N	N	Y	N	—	3	2	3	1	1	1	1	2	2	2	2	2	2	1	2	2
80	71	4	M	1	N	N	N	N	Y	N	DCMP	1+2	1	2	4	4	1	1	1	3	2	2	1	3	1	2	2
81	43	3	F	1+2+5	N	Y	N	N	Y	N	—	3	1	1	1	1	1	2	2	1	1	2	1	4	1	2	2
82	41	3	F	1+3	N	Y	N	N	N	N	—	3	2	2	1	1	1	1	2	2	2	2	2	4	1	2	1
83	47	3	F	1+2	N	Y	N	N	Y	N	—	3	1	3	1	1	1	1	2	1	2	2	1	4	1	2	2
84	28	2	F	1+3	N	Y	N	N	N	N	—	3	1	2	1	1	1	1	2	1	1	2	2	3	1	2	2
85	32	2	F	3	N	Y	N	N	N	N	—	3	2	2	1	1	1	1	2	1	2	2	2	3	1	2	2
86	49	3	F	1+3	N	Y	N	N	N	N	—	3	1	2	1	1	1	1	2	1	1	2	2	4	1	2	2
87	34	2	F	1+3	N	Y	N	N	N	N	—	3	2	3	1	1	1	1	2	1	2	2	2	2	1	2	2
88	43	3	M	2	N	Y	N	N	Y	N	—	3	1	1	2	2	1	1	1	1	1	2	1	3	1	2	2
89	38	2	M	3+5	N	Y	N	N	N	N	—	3	2	2	1	1	1	1	2	1	2	2	2	2	1	2	2
90	45	3	F	1+5	N	Y	N	N	Y	N	—	3	2	2	1	1	1	1	2	1	2	2	2	3	1	2	2
91	34	2	F	1	N	N	N	N	N	N	ASD	3	2	2	1	1	1	1	2	3	2	2	2	3	2	2	2
92	30	2	F	2+5	N	Y	N	N	N	N	—	3	1	1	1	1	1	1	2	1	2	2	2	2	1	2	2
93	35	2	F	3+5	N	Y	N	N	N	N	—	3	2	3	1	1	1	1	2	2	2	2	2	3	1	2	2
94	50	3	F	1+2+3+4	N	Y	N	N	N	N	—	3	1	2	1	1	1	1	2	1	1	2	1	3	1	2	2
95	44	3	M	3	N	N	N	N	N	Y	—	2	1	3	1	1	1	1	2	3	2	2	2	1	1	2	2
96	42	3	F	5	N	Y	N	N	Y	N	—	3	2	2	1	1	1	1	2	1	2	2	2	3	1	2	2
97	41	3	F	6	N	Y	N	N	Y	N	—	3	2	2	1	1	1	2	2	1	2	2	2	3	1	2	2
98	37	2	F	5	N	Y	N	N	Y	N	—	3	2	3	1	1	1	1	2	1	1	2	2	4	1	2	2
99	60	3	F	2	N	Y	N	N	Y	N	—	3	2	2	1	1	1	1	2	1	2	2	2	3	1	2	2
100	60	3	M	1+3	Y	N	N	N	Y	N	—	3	2	2	2	1	2	2	2	3	2	2	2	2	1	2	2